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THE CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

Gerald O. Strauch, M.D., ***Guest Editor***

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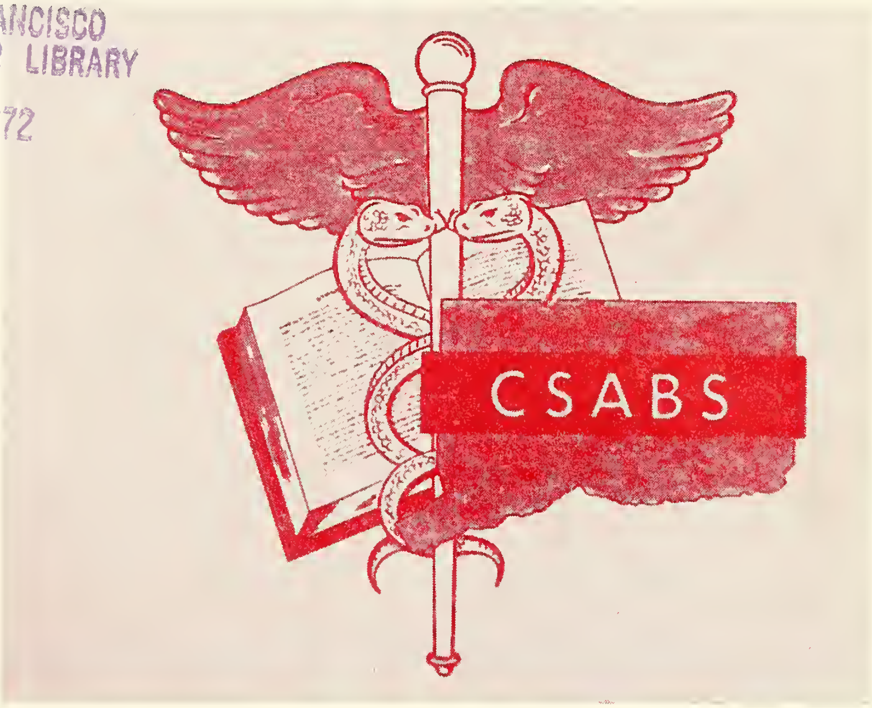

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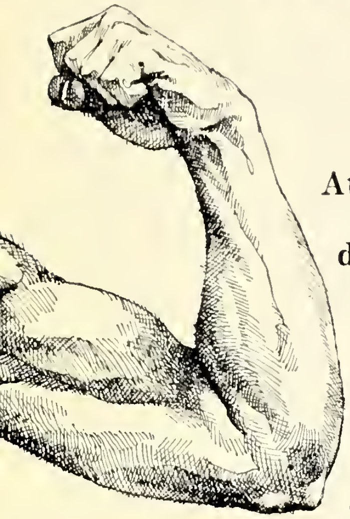
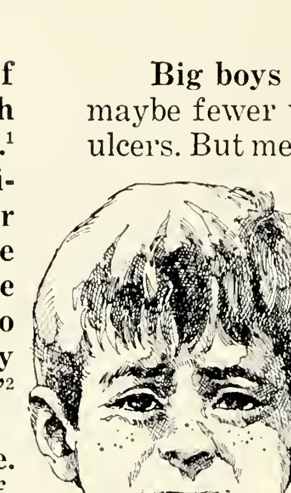
IF MORE MEN CRIED



At least seventy-five out of one hundred adults with duodenal ulcers are men.[1] Why? It may be significant that duodenal ulcer patients tend to crave recognition and are "especially vulnerable to threats to their manly assertive independence."[2]

Hypersecretion—an atavistic response. Stewart Wolf, who, with Harold G. Wolff, studied the personalities of duodenal ulcer patients, wonders if masculine competitiveness is related to "an atavistic urge to devour an adversary." It is striking, he reports, that an accentuation of gastric acid secretion and motility can be "induced in ulcer patients by discussions that arouse feelings of inadequacy, frustration and resentment."[2]

By chance? A lean, hungry lot. Was the link between emotions and gastric hyperacidity acquired through mutation to serve a purpose? During man's jungle period of evolution, the investigator points out, a male dealt with a foe by killing and devouring it. "It may be more than coincidence," he concludes, that peptic ulcer patients appear to be "a lean, hungry, competitive lot."[3]



Big boys don't cry. If more men cried maybe fewer would wind up with duodena ulcers. But men will be men—the sum total o their genes and what the are taught. Schottstaed observes that when mother admonishes he son who has hurt himsel that big boys don't cry, sh is teaching hi stoicism.[4] Crying is th negation of everythin society thinks of as manly A boy starts defending hi manhood at an early ag

Take away stres you can take away symptom

There is no question that stress plays role in the etiology of duodenal ulcer Alvarez[5] observes that many a man with a ulcer loses his symptoms the day he shuts u the office and starts out on a vacation. Th problem is, the type of man likely to have a ulcer is the type least likely to take lon vacations or take it easy at work.

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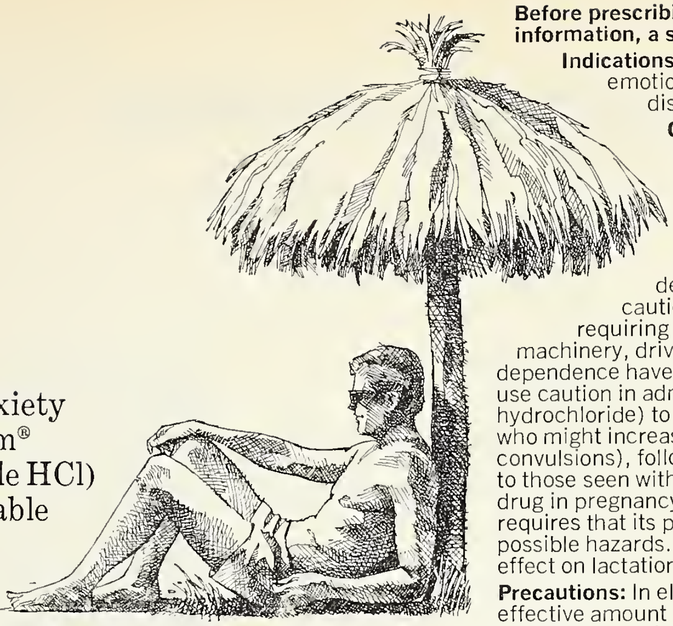

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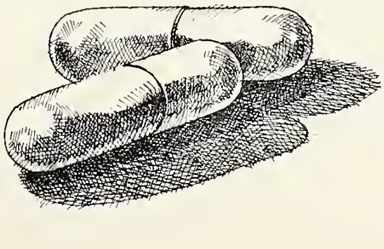

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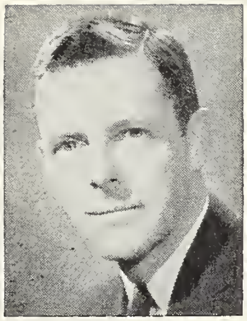
PRESIDENT'S PAGE



An obvious subdivision of health care planning about which so much is being written presently is health education. The public receives much information about the serious illnesses, the need for check ups, every conceivable kind of diet, and is admonished to get advice early in case of new lumps or symptoms. This may create anxiety in some patients' minds and no doubt contributes to the overuse of emergency room facilities by the "worried well".

While existing educational methods provide much useful information and some very advanced scientific knowledge about photosynthesis and DNA in high school biology courses, still there is needed some practical knowledge of the home care of minor injury and illness. Common sense is being pushed into the background by a feeling that there is someone who will take responsibility for deciding what to do about every abnormality.

I have talked to biology classes on various subjects and I believe this is an ideal place and time in a child's development to answer questions on health, physiology, principles of care, emergency first aid, etc. Students are eager for this kind of knowledge and readily assimilate it. At high school age it could be part of or separate from, biology (as not all students take that subject). The course should be given by enthusiastic doctors at not too frequent intervals so as to prevent boredom and allow time for thought and questions to come to the students' minds between sessions. They ask very intelligent questions. Proper answers would do much to clear up misconceptions, allay fears and counter rumors.

Local medical societies could set up a teacher panel and contact the local schools letting them know of the panel's availability. Beside furnishing health education for the student the doctor could also answer questions about careers in the health field. Interest stimulated by a doctor (or nurse) would be much more effective than that engendered by a brochure or pamphlet.

Education for adults should not be overlooked. No doubt most doctors find time for this on the occasion of the office visit for check-up or follow-up. This is most beneficial as it gives the patient the opportunity to clear up questions related to his particular problem. This extra effort makes for good public and private patient relationships and stimulates confidence in the depth of the doctor's knowledge of his subject. A patient with no doubts or fears unanswered is obviously less likely to criticize or find someone else to confide in.

Frederick C. Weber, Jr., M.D.
President

Late Complications of Duodenal Stump in Gastric Surgery

Gioacchino S. Parrella, M.D. and Nicholas A. Coassin, M.D.

Ever since Billroth[9] undertook "the pylorus tumor operation" in 1881, leakage of the duodenal suture line has been one of the recurring horrors of the gastric surgeon. In 1960 Welch and Edmonds[7] collected 281 cases of duodenal fistulae reported in the literature and pointed out that at Massachusetts General Hospital the incidence of fistulae following gastrectomy was 1.4 percent. None of these developed later than 11 days after surgery. They were associated with difficult turn-ins, edema, inflammation, pancreatic adhesions, and proximity of the ulcer to the bile ducts. Nine of 26 cases had proven pancreatitis. They concluded that the mortality from gastric or duodenal fistulae was 62 percent. Only one patient had a chronic fistula 8 months after gastrectomy. Schechter and Barrow[8] described fistulization 32 days after surgery. Bartlett and Lowell[2] reported 12 cases and pointed out the importance of performing an early jejunostomy for nutrition of the patient. Welch and Rodkey[10] preferred simultaneous jejunostomies for gastric decompression and jejunal alimentation. Chronic duodenal fistulae are caused by drains and best handled by operative treatment, according to Bohrer and Milici.[3] Brown, Speir and Trenton[4] and other investigators distinguished between end and lateral duodenal fistulae and correctly concluded that the former were less difficult to treat and in general resulted in fewer nutritional problems due to loss of fluids and electrolytes. Much has been written about the treatment of acute duodenal fistulae. Craighead and St. Raymond[6] and others[1,5] stressed the importance of skin protection, catheter suction at the fistula opening, jejunal feedings, parenteral fluids and suppression of upper gastrointestinal secretion.

The following two cases illustrate the pathogenesis, etiology and treatment of chronic duodenal stump fistulae and are unusual in that the fistulae developed ten and eighteen months after gastric resection. Because of chronicity, the management of these cases is surgical and is directed at the opening into the bowel.

Case I

G.I., a 58 year old factory worker, was admitted to the hospital April, 1969, with a five year history of intractable and recurrent ulcer pain associated with backache. At exploration a perforated pyloric ulcer was found with a small abscess in the gastrohepatic ligament. A Billroth II subtotal gastrectomy was performed, and the duodenal stump was closed by inversion using two layers. Pathological diagnosis was perforated chronic peptic ulcer of duodenum. Postoperative course was uneventful, and the patient was discharged on the 7th postoperative day.

Two and a half months later the patient was admitted complaining of upper abdominal pain and nausea. Physical examination revealed marked tenderness and spasm in the right upper quadrant with a suggestion of a deep mass. At exploration this mass proved to be a swollen, indurated pancreas and, at the junction between the head and the body of the organ, there was an area which was deeply fluctuant and which contained 15-30 ccs. of yellow-brown pus. The abscess cavity was drained with a sump, and the wound healed eventually without any fistula formation. He was discharged home on the 10th postoperative day.

On February 16, 1970, ten months after his original gastrectomy, the patient was admitted to the hospital complaining of shaking chills and severe backache. Abdominal examination revealed a tender right subcostal scar at the site of the second operative procedure, induration of the anterior abdominal wall, and a tiny fistula draining a small amount of greenish material. A gastrointestinal series showed a normally functioning gastrojejunostomy. On February 21, 1970, a catheter was inserted into the tract, and after injection of contrast medium on the operating table, it was shown that the dye immediately entered the duodenal stump. The duodenal stump perforation was identified at surgery and a #14 French catheter was placed into the opening and sutured in place. A sump drain was placed in the lesser sac. The duodenostomy tube was placed on suction, and minimal drainage was obtained. He was discharged home with the duodenal stump catheter in place. It was removed a month later, and there has been no fistulization since.

Case II

This 44 year old white male received a vagotomy, antrectomy, Billroth II gastrojejunostomy, and gastrostomy in September 1967 for intractable duodenal ulcer. Closure of the edematous stump was difficult, but a satisfactory inversion was obtained. Eleven days postoperatively, the day fol-

---

DR. GIOACCHINO S. PARRELLA, Chief of Surgery, Milford Hospital, Milford, Conn.

DR. NICHOLAS A. COASSIN, Attending Surgeon, Milford Hospital, Milford, Conn.

lowing removal of his gastrostomy tube, he suddenly developed acute epigastric pain, temperature elevation to 103°, and free air under his diaphragm by X-ray. The patient was treated with gastric suction and antibiotics for what was erroneously thought to be a leak from the gastrostomy site. He recovered uneventfully. He was readmitted for recurrent epigastric pain nine months later and a gastroscopy, gallbladder X-rays and gastrointestinal series were negative. His symptoms persisted, and eighteen months after his gastrectomy he was readmitted with intermittent episodes of right upper quadrant pain and fever. An incision and drainage of a presumed stitch abscess in his operative wound was performed, and subsequently this developed into a fistulous tract which discharged small bowel content. Upper gastrointestinal series revealed a peculiar change in the lesser curvature of the stomach, and injection of the fistulous tract showed that it emptied into a large pocket in the region of the duodenal stump and then into the stomach. At operation the fistula was followed into a chronic abscess near the duodenal stump. A second tract from this abscess pocket led into the gastric pouch 2.5 cms above the anastamosis. In order to evaluate the stump closure a jejunostomy was performed distal to the ligament of Treitz, and retrograde distention of the duodenum with saline demonstrated an opening in the stump. A duodenal and jejunostomy catheter was used to decompress the stump. Three weeks later he was discharged from the hospital with all tubes removed. He has had no recurrence of gastrointestinal symptoms in eight months.

Duodenal stump dehiscence is, in most instances, clinically obvious during the early postoperative period by changes in temperature and sudden appearance of abdominal pain and spasm. Those patients not subjected to surgical drainage either succumb to the problem or survive by developing a spontaneous fistula, usually through the operative wound. Although afferent loop obstruction is stated to be a cause of duodenal stump perforation, it did not seem to be a major cause in these two cases. The late development of the fistulae, the long periods of well being, and the lack of profuse drainage once the fistulae developed seemed to indicate other reasons for the complication.

Case II obviously perforated his stump on the eleventh day and responded surprisingly well to conservative management only to develop a fistula and a problem of major proportion eighteen months later. Immediate drainage in this case would have been the treatment of choice and might have avoided the late fistula development. It would appear that the fistula in Case I was the result of a postoperative pancreatitis with abscess formation even though there was no fever or amylase elevation. Closure of a difficult duodenal stump surrounded by inflammation could have resulted in vascular compromise of pancreatic lobules, necrosis, and abscess formation. Ordinarily, in either case, without immediate drainage, the results would have been disastrous except that the broad-spectrum antibiotics must have controlled the spread of peritonitis and localized the insult to a chronic abscess process. This then remained dormant an unusually long period of time before breaking forth into a duodeno-cutaneous fistula.

Perhaps more should be said for preventive measures. Currently drainage of an unsatisfactory duodenal stump closure is frequently done with either Penrose drains or sump drains. The consistent effectiveness of such a maneuver, however, remains to be demonstrated. On the other hand, although duodenostomy and jejunostomy seem to be a reasonable preventive measure, this method also carries with it its own complications. Obviously the surgeon will be guided by his assessment of the stump closure at the operating table and will take appropriate control measures.

Duodenal stump dehiscence should be thought of in every post-gastrectomy patient developing sudden abdominal pain and fever. Although drainage seems mandatory, an occasional case will apparently recover with massive antibiotics. Such cases may later become late fistula victims taxing the ingenuity of the surgeon as to how to diagnose the location of the bowel opening and how to effect closure of the fistula.

Summary

Two cases of late duodenal stump end fistula are presented. The late fistulization was undoubtedly brought about by vigorous antibiotic therapy at the time of acute perforation. Immediate drainage and decompression might have aborted the late complication. The treatment of choice of chronic duodenal fistula, in contradistinction to acute ruptures, is direct surgical attack at the point of opening into the bowel.

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Discussion of Dr. Parrella's Paper

Dr. Gerald O. Strauch, Stamford: We have encountered two problems which deserve mention in light of Dr. Parrella's interesting report.

The first was a middle-aged gentleman who had undergone subtotal gastrectomy six years prior to his autopsy, from which this specimen is shown. During the postoperative period he had developed a subphrenic abscess not thought to be associated with a duodenal stump leak. He came in six years later with severe abdominal pain, was explored at the Stamford Hospital. A large mass was found in the area of the head of the pancreas which was felt by the operating surgeon to represent a carcinoma. During his postoperative period he developed severe gastrointestinal hemorrhage and died. At autopsy the "pancreatic" mass was found to be a large pseudocyst, draining directly into the duodenal stump, and into which the gastroduodenal artery had bled. This pseudocyst was completely filled with hematoma, and his entire small bowel and G.I. tract was full of blood. This was evidently a duodenal stump blowout six years prior that had gone on to chronic abscess and pseudocyst formation, finally with hemorrhage into the pseudocyst, reconnection into the duodenum, and exsanguinating hemorrhage.

The second problem was a case of so-called Petersen's hernia, or the retro-anastomotic type of hernia that can occur following Billroth II's, usually in an antecolic type of anastomosis. As you see, what happens is that the afferent loop will herniate behind the stomach, with a twist of the gastrojejunostomy, and there is a closed loop obstruction of the duodenal stump. This particular case was a man who was ten years following gastrectomy and came into the Rhode Island Hospital. He stated at the time of admission that he had "never been guite right" since his gastrectomy, that he had had intermittent abdominal pain. He presented with severe abdominal pain, nausea, and vomiting without bile, and then developed a cystic abdominal mass in the left upper abdomen. This was treated with reduction of the hernia through the retroanastomotic opening, closure of the retroanastomotic hernia site, and anastomosis of the afferent limb to the efferent limb of the jejunum without enteroenterostomy, in other words, simple suture of the serosal surfaces to each other.

Dr. James H. Foster, Hartford: I enjoyed Drs. Parrella and Coassin's presentation but I would disagree with their primary thesis that a direct attack on a persistent duodenal stump fistula is the appropriate first step to take in the repair of these lesions. I would remind you of the old surgical principle that end fistulas heal without distal blockage, and a recent case emphasized the importance to us of remembering this dictum. After two or three attempts at closure of a duodenal fistula a young man was eventually referred to the Hartford Hospital a few months ago. He had undergone partial gastrectomy with jejunostomy and had intermittent drainage from his right upper quadrant of bile and duodenal contents ever since. Although barium contrast X-ray failed to demonstrate an afferent loop blackage, we felt that recurrent fistulization could only be explained on this basis and therefore made an approach to the gastrojejunostomy first. We revised this gastrojejunal anastomosis and simply ignored the fistulous tract in the right upper quadrant. The fistula stopped draining on the first post-operative day and has been closed securely in the approximate six month period since that operation. The principle here is that one must always look at the bowel distal to the fistula and prove that the lumen is widely patent, before a direct attack on any bowel fistula is made.

Morbidity and Mortality After Sigmoid Resection

Chester A. Wiese, Jr., M.D. and James H. Foster, M.D.

The occurrence of several anastomotic breakdowns following resections within a short period of time raised questions about their cause and actual frequency of occurrence. It seemed useful to review all sigmoid resections performed at Hartford Hospital for a two-year period, noting the number of breakdowns and deaths as well as their relationship, if any, to such measurable dimensions as age, level of the lesion, kind of bowel preparation, the operative technique, the use of decompressive procedures, diagnoses and the presence of significant associated disease.

The anastomotic technique employed, an estimate of the operative difficulty encountered by the surgeon at the time of resection, the management of anastomotic breakdowns, and the role of decompressive procedures were also recorded, and these results were compared with those of other similar series.

Definition

For the purposes of this study a sigmoid resection was defined as an anterior resection for carcinoma or benign disease of the sigmoid colon, the proximal rectum, or the recto-sigmoid colon with primary anastomosis. The level of the lesion was roughly determined from the measurements given by the sigmoidoscopist, the radiologist's decription of the barium enema, or by the surgeon's operative note. It was often only an approximation since the information was not always complete. Those that were judged to be at or below the peritoneal reflection were considered low, those above, high. All anastomotic leaks were verified by X-ray examination, by fecal drainage from the wound or by autopsy findings. Technical difficulties at the time of resection were considered to be dissection through inflamed or edematous tissue and anastomosis of bowel under tension or with edges of poor color.

Resuts

There were 161 sigmoid resections performed within the two-year period studied with 7 deaths, an operative mortality of 4.3%, and 17 anastomotic breakdowns, a rate of 10.6%. Seventy-seven patients were male and 84 female. The average age of the patients was 63 years, ranging from a one-year old infant with Hirschsprung's disease to a 92-year old man with volvulus. The hospital stay for all averaged 6 days preoperatively with a 3-week postoperative period. Those 90 patients who ran an uncomplicated course were in the hospital for 25 days whereas those who leaked and lived stayed longest —46 days, an increase of 84%. Those who leaked and died, or died with an intact anastomisis had a hospital stay of 23 days. The resections were performed by 27 surgeons, 4 of whom were residents. Fourteen of the 17 leaks were clinically evident by fecal drainage from the drain site or the operative wound; 2 were demonstrated by barium enema, and 1 was unrecognized before death but found at autopsy.

Eighty-seven resections were for carcinoma, 61 for diverticular disease, and the remaining 13 for an assortment of benign conditions such as volvulus and endometriosis (Table 1). Ten of the resections done for carcinoma had anastomotic leaks and 3 died, 1 of sepsis and 2 of unrelated causes. Of the 61 resections for diverticular disease, 7 leaked and 4 died, one of unrecognized intraabdominal hemor-

TABLE 1

SIGMOID RESECTIONS HARTFORD HOSPITAL JULY 1968-JUNE 1970

Diagnoses		
Adenocarcinoma		87
Diverticulitis		61
Others (All Benign)		13
Volvulus	5	
Endometriosis	4	
Stricture	1	
Hirschsprung's Disease	1	
Polyposis	1	
Sigmoiditis	1	

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rhage at the site of a transverse colostomy performed for diversion, and 3 of unrelated causes.

Ninety-four resections of the series were considered technically "easy." Of these, 9 leaked, a rate of 9.5%. Eight of the 67 "difficult" resections leaked, or 12%.

Ninety-one of the lesions were considered low, that is at or below the peritoneal reflection. Twelve patients with low lesions leaked, 2 going on to die, 1 because of the leak and 1 of liver failure. Of the remaining 70 patients with high lesions, 5 leaked and of these 2 died, both probably attributable to the leak. Three other patients with high lesions also died, but of unrelated causes (2 cardiac deaths and 1 renal failure).

None of the 13 patients who had disease other than cancer or diverticular disease suffered a postoperative anastomotic breakdown or operative death. The lesions in these patients were about evenly divided as to level and difficulty of resection.

Eighty-seven patients were found to have associated disease such as arteriosclerotic heart disease, diabetes, cirrhosis, emphysema, distant metastases, or some condition requiring steroid therapy. Seven patients with significant associated disease died and 16 suffered dehiscence of the anastomosis; 2 deaths were clearly attributable to the anastomotic leak, 1 of sepsis and 1 of hemorrhage. Of the 5 unrelated deaths, 2 were cardiac, 1 renal failure, 1 liver failure, and 1 from pulmonary embolism on the eighth postoperative day. At autopsy this last patient was found to have an unrecognized anastomotic leak which may have been associated with the source of the embolus, thereby relating the leak to the death. None of those 74 patients in which there was no associated disease died and only 1 suffered an anastomotic breakdown.

Management Of Anastomotic Leaks

Table 2 outlines the methods of management in the 16 patients with clinically recognized anastomotic leaks after sigmoid resection. The seventeenth leak was not recognized until autopsy following death by pulmonary embolism.

TABLE 2

MANAGEMENT OF LEAKS

Local Drainage		7
Closed Spontaneously	5	
Discharged Draining	1	
Died (Unrelated Causes)	1	
Preoperative Decompression		2
Discharged Draining	2	
Proximal Transverse Colostomies		7
Discharged With Colostomy	5	
Died (Due To Leak)	2	

Local drainage alone resulted in the healing of anastomotic breakdowns prior to discharge from the hospital in 5 patients. In addition to these 5 patients, 1 was discharged still draining from a leak without treatment because he was known to have pulmonary metastases, and 1 other patient with a leak died of liver failure without further surgey.

Two patients whose anastomoses leaked had had preresection decompression and were discharged with no further treatment still draining.

The 7 remaining patients who developed anastomotic dehiscences had proximal colostomies performed for the leaks, and of these 2 died because of the leak. The remaining 5 patients went home with functioning colostomies.

Relationship Of Proximal Decompression To Anastomotic Leaks

Nineteen patients had a proximal colostomy done from 17 days to 15 months prior to sigmoid resection. None of these colostomies was closed at the time of resection (Table 3). One patient in the group suffered anastomotic breakdown. Five patients with cancer and 2 with diverticulitis underwent cecostomy 7 to 26 days before resection, and 1 of these patients also developed a leak postoperatively in spite of continued cecostomy drainage.

None of the 8 patients who had proximal colostomy or the single patient with cecostomy done at the time of resection suffered a subsequent anastomotic breakdown.

Anastomotic Techniques

The end-to-end two layer anastomosis using catgut for the mucosa and silk for the serosa was utilized in 146 patients' anastomoses, 10% of which leaked. Eleven anastomoses were the end-to-end one layer technique, 9% of which leaked and there were 4 end-to-side two layer anastomoses, one of which leaked. All patients had some sort of mechanical bowel preparation, but neither the kind of anti-

TABLE 3

ROLE OF PROXIMAL DECOMPRESSION

Done Preresection	
Transverse Colostomy	19
1 Leaked	
1 Died (Unrelated)	
Cecostomy	7
1 Leaked	
1 Died (Unrelated)	
Done With Resection	
Transverse Colostomy	8
Cecostomy	1
(None Leaked or Died)	

biotic used nor its omission altogether caused any change in the complication rate.

In the Hartford Hospital series 7 surgeons did over half the resections, while a majority of the surgeons did an average of about 5 resections every two years. One surgeon had 3 of his anastomoses break down and 2 of his patients die. Twenty resections were done by four residents with 3 leaks and 1 death.

Discussion

Table 4 compares this Hartford Hospital experience with other reports. This comparison with other series is somewhat hampered by the fact that each author publishes with some specific project in mind, tending to bias the results. For example, Goligher's[1] high rate of 51% for anastomotic breakdowns arises from his practice of actively searching for leaks even in the absence of clinical evidence of their existence. In his series of 73 sigmoid resections, all of his patients on the tenth to twelfth postoperative day underwent digital rectal examination and sigmoidoscopy. The presence of blood or pus upon the finger or scope, or gaps in the suture line were considered evidence of anastomotic breakdown. On the fourteenth postoperative day all the patients were subjected to low-pressure, small-volume barium enemas, many of which revealed unsuspected leaks. The operative mortality in his series was only 5.4% in spite of the high leak rate. Goligher also pointed to the work of Bell & Lewis[4] in London who suggested that the practice of administering neostigmine at the conclusion of the resection to reverse the effects of curare exposes the anastomosis to considerable strain if the accompanying dose of atropine is ill-timed.

Palumbo's[2] study in the Veterans Hospital at Des Moines was a comparison of the mortality rates of abdominoperineal with anterior resections. He reported an operative mortality of 6.5% but he made no note of complications. At Albert Einstein, Adam's[5] figures for low colorectal anastomoses after resection for carcinoma alone showed an operative mortality of 11.1%, with 7.7% of the anastomoses breaking down.

TABLE 4

SIGMOID RESECTIONS

		Cases	*Deaths*	*Leaks*
Hartford Hospital	— 1970	161	4.3%	10.6%
Goligher Leeds	— 1970	73	5.4%	51. %
Palumbo Des Moines	— 1968	76	6.5%	
Adam Albert Einstein	— 1967	117	11.1%	7.7%
Herter & Slanetz Presbyterian	— 1967	263	6.5%	12.5%
Vandertoll & Beahrs Mayo	— 1965	1766	4.2%	31.6%
Whitaker London	— 1968	615		16.4%

Herter & Slanetz,[6] in a larger series from Presbyterian Hospital in New York City, were studying the influence of antibiotic bowel preparations on the patients' postoperative course. Two hundred sixty-three of their patients underwent anterior resections for which the operative mortality was 6.5% with 12.5% of the anastomoses leaking. The authors concluded that the operative mortality was the same whether or not an antibiotic prep was used. Vandertoll & Beahrs[8] at the Mayo Clinic have one of the largest series of anterior resections, 1766 cases, of which 31.6% leaked and 4.2% died. In an editorial in 1966, Beahrs[7] stated that ideally the operative mortality for low anterior resections should be 5% or less. He recommended careful selection of patients, meticulous surgery, end-to-end anastomoses with two layers, suction drainage, and an antibiotic prep. In the Hartford Hospital series there was no correlation between complications and the use of antibiotic preps, the type of anastomosis or the suture material used.

Whitaker,[3] in his London series, was interested in measuring the blood flow in the inferior mesenteric artery after ligation at different levels and observing its influence on the healing of colonic anastomoses. After computerizing the results of 615 cases from three hospitals he found an anastomotic leak rate of 16.4% and concluded that high ligature of the inferior mesenteric artery does not contribute to anastomotic breakdown, but that in very low lesions the older the patient, the more hazardous the resection.

In the Hartford Hospital series there was no correlation between age and complications. As would be expected, hospital stay was increased significantly by the complication of an anastomotic leak. Technical difficulties encountered at operation did not seem to influence the complication or death rate. The rate of dehiscence for low anastomoses was twice that of high anastomeses. The rate of anastomotic breakdown was approximately equal for resections done for cancer and diverticulitis. Proximal decompression done prior to sigmoid resection did not provide secure protection against anastomotic leak, but no leaks occurred in this series after synchronous proximal decompression.

One of the most consistent and striking features of this study was the close correlation of complications with associated disease. Almost 20% of those patients with associated disease suffered an anastomotic breakdown and 9% died, whereas in 74 patients without associated disease, there was no mortality and only 1 anastomotic leak. Thus significant associated disease does represent a serious threat to the patient undergoing anterior resection of the sigmoid colon, and its presence should be a clear warning of trouble ahead. Therefore in addition to the usual indication for prophylactic decompressive procedures ordinarily based upon the color of the bowel or technical difficulties encountered at the time of the anastomosis, perhaps the presence of significant associated disease in itself is reason enough to perform prophylactic decompression. None of the 8 patients who had a decompressive procedure performed at the time of the resection died or suffered anastomotic dehiscence.

Conclusions

From a retrospective study of 161 sigmoid resections at Hartford Hospital over a two-year period it may be concluded that sex, age of the patient, diagnosis, level of the lesion, and technical difficulties encountered at the time of operation do not substantially influence the complication or mortality rate of the operation. Significant associated disease does, however, markedly increase the mortality and complication rate. Its presence alone should be an indication for prophylactic decompression of the bowel. Finally, anastomotic breakdown need not be fatal if recognized and adequately treated. In the Hartford Hospital series there was no apparent statistical association between anastomotic leaks and death.

Treatment usually will include proximal colostomy, but in a patient without systemic manifestation of toxicity, controlled local drainage may provide a satisfactory outcome.

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Discussion Of Dr. Wiese's Paper

Dr. William A. Whalen, Willimantic: I want to thank the authors for allowing me to read the manuscript in advance. This allowed for a very brief survey of 64 of our personal cases of sigmoid resection which were performed over the last eight to ten years. On this basis I would like to draw a few comparisons, Dr. Wiese. In general, we discovered, as did Dr. Wiese, that the anastomotic leaks did not appear to be directly related to the location of the lesion, the degree of difficulty of the procedure, the type of bowel prep employed, or the technique of closure utilized. The sampling was comparable as far as age and sex was concerned. In our small group of patients, diverticulitis predominated the composition of the series. There were 59% of the patients with diverticulitis and 36% with carcinoma. The mortality in our group was 6.2%, a little higher than Dr. Wiese's series. This is four out of 64 cases; and there were four anastomotic leaks with an incidence of 6.2%. In two of the patients where the anastomotic leaks occurred, associated disease was present. Metastatic disease was present in the liver in one, and in the second patient, the patient was an obese smoker with advanced pulmonary disease. The two remaining leaks occurred in patients with very complicated problems. Both had undergone a previous transverse colostomy and drainage of a pelvic abscess six months prior to their definitive resection, and both individuals survived the leak without drainage procedures being performed. One returned for reresection and died in the postoperative phase. As far as death was concerned, two of the deaths were definitely related to leaks. Metastatic disease of the liver was present in two, and the other patient died of hepatic failure. 13 transverse colostomies were performed in these 64 patients, and two out of the 13 leaked in spite of the transverse colostomy being present. 25 underwent complementary cecostomy, and 28 individuals underwent sigmoid resection without decompression. It appears to me that there is no doubt that on the basis of Dr. Wiese's study and our very brief investigation, that associated diseases have a direct effect on the morbidity and mortality following sigmoid resection, or other procedures, for that matter.

Arbitrarily dividing our sampling into two groups, as Dr. Wiese did, even with the ideal good risk patient and the poor risk patient, with less ideal operating conditions, it was discovered that in the ideal or good risk patient no leaks or deaths occurred in our experience. In the so-called poor risk patients, 75% of the patients were carried through the surgical procedure successfully, and in the remaining 25%, anastomotic leaks with or without death occurred. So the problem here appears to be able to select the one out of four individuals where a transverse colostomy might be of assistance in preserving the suture line. In our experience, however, the addition of transverse colostomy does not always guarantee the integrity of the suture line. Certainly if one anticipates poor healing, if incomplete obstruction of the proximal bowel with edema is present, or if the adequacy of the anastomosis is questioned, in the presence of associated disease, the transverse colostomy would appear indicated. Simultaneously we are all aware of the importance of the proper blood supply of the suture line, that all tissue along the entire length of the thickened bowel should be removed, and finally that no tension should be present on the suture line in order that a water-tight anastomosis should be performed. Finally, in conjunction with the discussion, I would like to mention the technique that was advocated many years ago by Dr. Harvey which involves the use of cecostomy in decompressing the patient for definitive sigmoid resection. It is specifically useful in the presence of large bowel obstruction secondary to a left-sided lesion of the colon where a diagnosis of carcinoma has been previously made by barium enema or sigmoidoscopy. A McBurney incision can be made with removal of the appendix and the insertion of a large calibered #36 multiperforated red rubber catheter through the appendiceal stump if the appendix has been removed. This can be advanced to the hepatic flexture. At the time of the procedure the diagnosis can be verified by palpation, and, postoperatively, a Y-tube irrigation set-up is connected to the cecostomy tube. Daily irrigations performed through the tube after 36 hours are instituted, and bowel prep can be done. The patient can be nicely decompressed and prepared for definitive resection in one week. This is one instance where cecostomy is indicated, emphasizing that the cecostomy is of value only in short term decompression. We utilized this in a number of the patients in our series with great success.

I want to compliment the authors on their presentation, and I appreciate the opportunity of reviewing and commenting on the paper.

Dr. John B. Ogilvie, Stamford: They have done something in Hartford Hospital which I think many of us, including myself, ought to do; and that is to take the time and put the effort into making a self-analysis of our tragedies and failures rather than limiting our papers to triumphs. As I read this paper over, the thing that impressed me was that only the leaks which led to trouble were of major importance. When I was trained in New York Hospital, back in the '30's, we were much more conservative, and we were trained to do most of the left-sided resections of the colon in three stages. We very seldom did them in one stage, so I have become used to doing at least a two- or three-stage operation, and I have been impressed that we did not get as many leaks as we do now. However, in thinking back on my own cases recently, I have also personally had the leaks and disruptions of anastomoses done even in the presence of a proximal colostomy done one or two weeks prior to that. One thing that I have noticed. Prior to closing a colostomy, I routinely do a barium enema or a Gastrografin study approximately two or three weeks after the anastomosis is done, and this is in asymptomatic patients. A high percentage of those people will show a leak without any symptoms at all. I am reminded of one I did about three years ago for diverticulitis. A year later she came back in the hospital for something else regarding her kidney. Her medical man got a barium enema, and she had a fistulous tract which was a good 6 to 8 inches in length with no bowel disturbance whatever, no fever, no abscess, and completely asymptomatic. Of course we did nothing about it. I have a suspicion that many more of these leak if we carefully investigate them.

One thing I would like to ask Dr. Wiese—obviously after a leak is discovered, doing a proximal colostomy doesn't cure them all. Has anyone carried out a direct attack on the anastomosis itself? I am reminded of this because of the fact that a ruptured diverticulum for which we do a proximal colostomy still carries in itself a high mortality rate, and some people have suggested, as you know, that perhaps attacking the diverticulum and the rupture itself, at least in that area, is justified.

I enjoyed the paper.

Dr. Wiese: I find no evidence of anyone's attacking the anastomosis, after it had broken down, directly—at least not in our series, and I didn't run across it in the literature.

Central Venous Feeding: A Call for Caution

Lawrence K. Pickett, M.D.

One of the major advances in supportive care for surgical patients was initiated and popularized by Dudrick and Wilmore[1,2] and has since been espoused on many fronts by many people. There is no question that the ability to offer total nutrition, and thus positive nitrogen balance, to the individual who does not or cannot take sufficient nutrition by mouth is a tremendous boon to the surgeon. Positive nitrogen balance contributes to wound healing, helps combat sepsis, and in general can make successful an otherwise hopeless plight.

In the field of pediatrics utilization of this modality has been increasingly popular. There has been enough experience now to evaluate and be critical of its exact indication and to make some comment on the proper uses and abuses of the method.

As indications for its use one can point to any individual who is unable to support nutrition by the gastrointestinal route for a prolonged period of time. This would certainly include such conditions as atresias with loss of intestinal substance, mid-gut volvulus, large omphalocele or gastroschisis where a staged procedure must be done to accomplish closure, severe and intractable diarrhea, perhaps secondary to enterocolitis, or other devastations secondary to infection. In older children granulomatous colitis and ulcerative colitis needs support during the acute phase and during the crises. This list could be continued to include most any condition in which the use of the alimentary canal was temporarily impossible.

Technique

The technique for the introduction of these central feeding lines will not be dwelt upon. Needless to say, the percutaneous route, common in the adults, is frequently impossible in children due to their size. One is, therefore, forced to use a very small silastic catheter introduced to the external or internal jugular vein under most careful asepsis. The tip of the catheter should be advanced to the superior cava and checked there radiologically to be sure it is correctly placed. The catheter-skin junction and the cathetervein junction should be separated by at least five to eight centimeters so that a bridge is established to protect against infection. The care of the catheter-skin junction must be most meticulous with dressing changes daily or every other day using an iodine scrub for the skin and antibiotic ointment for the area with an occlusive dressing. Also included in the line should be a millipore filter, though this has been abandoned by many. The preparation of the solutions leave many opportunities for sepsis. The material itself is a superior culture medium for fungi as well as bacteria.

No one standard preparation is obviously adequate since many of the tiny infants will be bothered by the hyper-osmolarity of the solution when first introduced and will have a tremendous osmotic diuresis if a too concentrated solution is used initially. Careful introduction of a solution that may be inadequate for total caloric needs precedes progressive increase in the caloric content, until almost one calorie per milliliter is obtained. Because of the relatively small amounts that need be introduced into infants, the use of a constant infusion pump is essential for uniform deliverance of the material over a twenty-four hour period.

It is also important to use a central line only for feeding purposes and not to interrupt the system frequently for withdrawing blood samples, as this adds an unnecessary risk of infection. Likewise, when there are additional losses and electrolyte depletion, replacement is best accomplished through a separate line and not in the central feeding line.

Complications

The complications of the system now appear in the literature in frequent articles; one of the most common is obviously that of sepsis, and candida sepsis is the most frequent form of contamination. Diffuse candidiasis has been encountered on a number of occasions as evidenced by the article by Ashcraft,[3] et al. This has served in many series as the chief threat to the survival of the patients. Bacterial infection can be found by blood cultures. If septicemia is noted the catheter must be withdrawn until infection has been cleared. Aside from sepsis, one of the major pitfalls is the need to introduce Vitamin K. As this is not available in the

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starving individual, it must be given intra-muscularly or in the solution on a regular basis. Some authors have felt that trace lipids and other elements can be added by using plasma transfusions once or twice a week. This is not agreed by all as being necessary. The absence of lipids from the material does not seem to add any additional problems even over a prolonged period of time.

Summary Of Our Experience

The table presents the experience in a selected group of twelve cases in which the method was used for a prolonged period of time. Equal numbers have lived and died. The cause of death in general has been sepsis, though not necessarily related to the method.

Favorable Case for Method

J.C., a 2440 gram infant was born with gastroschisis and two evident areas of atresia of the bowel, one in the upper ileum and one in the transverse colon.

Central venous feeding was introduced during a multiple-staged repair of the gastroschisis, accomplished in seven days. Following the removal of the silastic used in the repair of the abdominal wall, the ileal atresia was repaired by direct anastomosis and the colonic atresia treated by Mikulicz colostomy. Satisfactory gastrointestinal function was established by the 17th day of life and central feeding was discontinued. Weight of baby when oral alimentation was supporting the child was 2520 grams, indicating satisfactory support and positive nitrogen balance for wound healing.

Unfavorable Case for Method

R.R., a 6 lb. 4 oz. infant, was born with a distended abdomen and evidenced intestinal obstruction in first 24 hours. Operation at a regional community hospital revealed evidence of mid-gut volvulus and destruction of a massive amount of intestine. An anastomosis was accomplished which functioned. Severe diarrhea resulted and the baby was transferred to YNHH for central venous feeding. Barium enema at this hospital revealed that the anastomosis had been made between midtransverse colon and fourth portion of the duodenum. Recovery of sustaining gastrointestinal function was deemed impossible even by the most optimistic

RESULTS OF LONG-TERM "INTRAVENOUS HYPERALIMENTATION"

Survivors Case	*Diagnosis*	*Primary Operation*	*Indication for Intravenous Hyperalimentation*	*Total Intravenous Nutrition*			
				Age At Start (Days)	*Duration (Days)*	*Weight*	
						At Start	*At End*
1.	Hirschsprung's Disease	Jejunostomy	Inanition	83	120	2505	4390
2.	Esophageal Atresia Duodenal Atresia	Duodeno-jejunostomy Staged repair of esophageal atresia	Bowel decompression	8	20	1780	2110
3.	Gastroschisis	2-stage repair	Intestinal obstruction Bowel decompression	4	16	1730	1990
4.	Extreme prematurity	None	Inanition	11	16	600	725
5.	Hirschsprung's Disease	Ileostomy	Inanition	28	26	1980	2300
6.	Gastroschisis Atresia of bowel	Staged repair Repair	Intestinal obstruction Bowel decompression	2	15	2440	2520
Non-Survivors							
1.	Malrotation Mid-gut volvulus	Jejuno-colostomy (Mikulicz)	Inanition Chronic intestinal obstruction	42	15	1860	2150
2.	Malrotation: Mid-gut volvulus	Jejuno-colostomy	Inanition	26	40	3190	3875
3.	Gastroschisis	2-stage repair	Intestinal obstruction Bowel decompression	29	38	1660	2185
4.	Mid-gut volvulus (Ante-natal)	Duodeno-ileostomy	Chronic intestinal obstruction Inanition	3	63	2840	4000
5.	Mid-gut volvulus (Ante-natal) Cystic fibrosis	Jejuno-ileostomy	Chronic intestinal obstruction Inanition	5	105	1420	3000
6.	Recurrent TEF	Esophageal anastomosis	No oral feedings Recurrent aspiration pneumonia	107	30	3060	4000

of the observers. Central feeding was not used. The baby died in seven days.

Summary

Central venous feeding is a tremendous advance in supportive care for both medical and surgical patients, particularly in infancy and early childhood. The method does, however, carry with it a certain risk of sepsis. Complications related to the method itself make selection of the patients an exceedingly important matter. One of the features noted by the series presented from the Yale-New Haven Hospital is the possibility that one might support a child for a prolonged period of time, with great expense to the family, both in money and emotional outlay, and false hope when there is no chance of restoring this child to a functional state. We as practioners may be lulled into a false sense of security by the method which can totally support an individual. We must look with great care and caution at the possibility of restoring gastrointestinal function. If one can be sure that there will be adequate compensatory hypertrophy of the remaining intestine through villus hypertrophy and elongation, resulting in the ultimate ability of the patient to sustain himself without extra support, the method certainly should be used. If, however, there is very little chance that this individual could ever attain any form of gastrointestinal self-support, in the absence of a satisfactory method of intestinal transplantation it is both immoral and wrong to introduce this method under such circumstances. Properly used, with the proper precautions, this will save many lives. It may, however, contribute to one of the major problems of the day, that of artificial support of life which is impossible without the supporting mechanisms. Yet another perimeter in difficult decision making has been introduced.

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Discussion Of Dr. Pickett's Paper

Dr. Gerald O. Strauch, Stamford: I would like to pose one question here on the subject of "intravenous hyperalimentation" in general. I am told by the people who are detailing the commercial stuff that they are doing a landslide business in hyperalimentation kits. I find this a little bit difficult to believe, but it may be so. I would just like to ask how many people here have been conducting current cases with total central venous alimentation in the truly modern sense? One may feel out of the mainstream of surgery these days if he is not running at least one intravenous hyperalimentation regimen on some patient at all times, and I don't believe this is a realistic impression. It is a little comforting to see fewer hands than the detail men would imply. Dr. Pickett, do you have any further comment in this regard?

Dr. Ira S. Goldenberg, New Haven: With regard to the problem of the association of sepsis with prolonged intubation, the slides that you showed demonstrated that intubations in your group of cases varied from a very short time to a very long time. What is the magic "too long," or when is the time beyond which you think this thing can't be pursued?

Dr. Pickett: When you get sepsis you have been too long! The length of time simply introduces another factor of sloppy care of the bandage and the skin-catheter junction. The longer a child is there, the less expertise is involved, and the more chance there is for introduction of sepsis. Generally when the procedure is prolonged there are other elements contributing to sepsis, such as bowel troubles and intra-abdominal sepsis. Any time you have distant sepsis, the catheter, being a foreign body, picks it up and you have this as a problem. So that I think there is no magic time, but the longer the catheter is there, the more people get relaxed in taking care of it. We really have to zero in on one person's doing the dressings every other day, using occlusive dressings, washing the wound with Betadine, applying an antibiotic ointment, and with no break in technique whatsoever.

Dr. Goldenberg: This is the point I wanted to emphasize. As Dr. Strauch indicated, widespread use is now imminent. One of the important things is who is actually taking care of the equipment after it is in place, and I think that the people who talked about this before have emphasized what you emphasized now—that one person ought to be responsible for it and make sure that it is done properly, and that we don't get sloppy as time goes by and allow sepsis to be introduced.

Dr. Lee H. Ellison, Hartford: Are there other options besides subclavian vein or jugular vein catheterization available in premature infants?

Dr. Pickett: We have been driven to the wall with some of these children who have had four and five replacements. We do external jugular and internal jugular on both sides and then try to get into the subclavian notch into the subclavian. These are very tiny vessels in tiny prematures and you ought to be taking your feedings well before you start to put one in. But there are other options. We have not had any success from below at all because of the trouble with arterial spasm.

Dr. Strauch: Dr. Tom Randall, I am sure, is going to discuss elemental diets tonight as a sort of in-between measure between regular enteral feedings and central venous alimentation. Do you think there is any place for this in the kids?

Dr. Pickett: We were very discouraged with Codelid and all the other things in children. We have tried it on kids, and we have tried it on rats, and we don't see that there is any great advantage in this intermediate stage, but I am sure there is. We have used an elemental diet with short chain triglycerides and hydrolized protein and this has sort of filled the same bill but it hasn't been the Codelid that we used in this series.

Dr. Charles J. Middleton, Hartford: One point that Dr. Dudrick makes in talking about hyperalimentation is that the intravenous tubing and all the connections must be kept meticulously free of contamination and that this line should not be used for the withdrawal of blood samples or the administration of any intravenous medications. How do you get around this problem in your cases?

Dr. Pickett: We have a superior house staff with less of a tremor than I have, and they can get blood from other places. We do not allow this line to be opened at all, particularly distal to the Millipore filter in the line. If it is opened proximal, then that whole solution is thrown away because it has been found that Candida grows exceedingly well in this. Even in the uncontaminated solutions you see a little cloudiness occasionally. We don't use this system at all for blood withdrawal. If we did, we would expect to get into trouble.

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Complementary Gastrostomy: A Personal Series Without Complication

Gerald O. Strauch, M.D.

Gastrostomy as an adjuvant in the management of selected surgical patients has become well established during the past two decades. Testimonials to its ease of performance, effectiveness as an alternative to nasogastric intubation, simplicity of management, and acceptance by patients are included in almost any comprehensive consideration of serious abdominal surgical problems.[1-4] Earlier experience with complementary gastrostomy reported by some investigators was associated with unacceptable morbidity and even mortality;[5] however, the realization that meticulous attention to technique and management of the gastrostomy in properly selected patients can reduce its complications to negligible levels has prompted many surgeons to use it frequently. The series presented here involved no untoward events which could be identified as related to the performance or presence of the gastrostomy. Since these cases were all under my personal care, it was felt of interest to relate this experience.

Case Material

Seventy-eight gastrostomies were performed on 75 patients during a period of ten years from January 1, 1961, to October 31, 1970. All operations were performed or directly supervised by me. Eleven gastrostomies were in children and 67 in adults (Figure 1.), ages ranging from less than twelve hours in three newborns to the tenth decade in one elderly lady. One-third of the patients were elderly. Three adult patients required operative procedures on two occasions, gastrostomy being utilized in each instance.

The indications for gastrostomy in this study are seen in Figure 2. A combination of indications resulted in the decision for gastrostomy in 28 instances (36 per cent).

Figures 3-9 list briefly the nature of each case and denote cases resulting in death. As can be readily appreciated, the majority of cases involved here were complex management problems. Four cases have been described in other reports.[6-8]

Death within 30 days following operation occurred in eight instances (10 per cent). Figure 10. lists other complications in the series which are of apparent interest in a study of this type.

Technique Of Gastrostomy

The modified Stamm gastrostomy used by the late Dr. J. Murray Beardsley as a complementary procedure was taught to me during my residency at the Rhode Island Hospital. (Eight gastrostomies in this study were included in the review of 478 gastrostomies from the Rhode Island Hospital in 1964.)[9] The technique presently used is as follows, and differs little in principle from that described by Beardsley.

Following the completion of the primary operation and prior to abdominal closure, the anterior gastric wall is exposed and grasped with Babcock forceps. A pursestring suture of 0 chromic atraumatic catgut is placed in the seromuscular coats of the stomach wall approximately midway between the greater and lesser curvature, at the junction of the middle and distal thirds of the organ.

The anterior abdominal wall wound edge is elevated, and the peritoneum and musculofascial layers of the wound are grasped with a Kocher clamp. At a point in the abdominal wall overlying the normal location of the site of the gastric pursestring suture, and at least four centimeters from the main incision, a small stab wound is made in the skin. The tip of a Foley catheter is drawn through the abdominal wall via a tunnel created directly through the abdominal wall by passage of a large Kelly clamp through all abdominal wall layers at the site of the stab wound. A No. 22 Foley catheter is ordinarily used in adults, with corresponding smaller sizes being used in children and infants.

A small serosal incision is made in the gastric wall within the previously placed pursestring stitch, and the gastric wall is then bluntly perforated with a hemostat, the tip of the Foley catheter being introduced into the gastric lumen through the perforation. The pursestring suture is tied around the catheter, and the ends are cut.

A second concentric pursestring suture of 0 chromic catgut is placed one centimeter peripheral to the first. Using a hemostat, grasping the cut ends of the first pursestring, to invert the gastric wall at the site of catheter penetration, the second pursestring stitch is tied and cut.

DR. GERALD O. STRAUCH, Attending surgeon, Stamford Hospital and St. Joseph's Hospital, Stamford, Conn.

FIGURE 1

COMPLEMENTARY GASTROSTOMY

78 Cases

ADULTS			67
CHILDREN			11
INFANTS		6	
NEWBORNS	4		

FIGURE 2

COMPLEMENTARY GASTROSTOMY

Indications

1) COMBINATION		28
2) ANTICIPATED PROLONGED ILEUS		20
MAJOR GI CANCER OPERATION	6	
MAJOR ABDOMINAL TRAUMA	5	
MAJOR AORTIC SURGERY	4	
3) ANTICIPATED GASTRIC ATONY		14
VAGOTOMY	11	
4) MAJOR PEDIATRIC GI SURGERY		8
5) INTOLERANCE FOR NASOGASTRIC TUBE		3
6) ESOPHAGEAL RUPTURE OR INJURY		3
7) AGED OR DEBILITATED PATIENT		1
8) PULMONARY DISEASE		1
HEAVY SMOKING		
9) GASTRIC FIXATION		

FIGURE 3

COMPLEMENTARY GASTROSTOMY IN CHILDREN

Newborns (4)
  **CONGENITAL DIAPHRAGMATIC (BOCHDALEK'S) HERNIA (2)
  DUODENAL ATRESIA; DOWN'S SYNDROME
  **TRACHEOESOPHAGEAL FISTULA WITH ESOPHAGEAL ATRESIA; IMPERFORATE ANUS; TETRALOGY OF FALLOT
Infants (2)
  SEGMENTAL ILEITIS WITH GENERALIZED PERITONITIS
  CORRECTABLE BILIARY (COMMON BILE DUCT) ATRESIA
Children (5)
  RUPTURED APPENDICITIS WITH PROXIMOLATERAL CECAL DYSTOPIA (2)
  SMALL-BOWEL VOLVULUS DUE TO ADHESIONS
  TRAUMATIC EVISCERATION
  *MIXED CELL CARCINOMA OF LIVER (RIGHT HEPATIC LOBECTOMY)[6]

*PREVIOUSLY REPORTED
**ONE DEATH

FIGURE 4

COMPLEMENTARY GASTROSTOMY IN ADULTS

Esophageal Cases (3)

ESOPHAGEAL DISRUPTIONS (3)
  *SPONTANEOUS SUBPHRENIC RUPTURE[7]
  ***IATROGENIC PERFORATIONS (2)

*PREVIOUSLY REPORTED
***TWO DEATHS

FIGURE 5

COMPLEMENTARY GASTROSTOMY IN ADULTS

Gastroduodenal Cases (30)

ACID PEPTIC DISEASE (22)
  MASSIVE HEMORRHAGE (3)
  OBSTRUCTION (3)
  RECENT PERFORATION (3)
  RECENT PERFORATION AND MASSIVE HEMORRHAGE
  RECENT PERFORATION AND OBSTRUCTION
  ACUTE PERFORATION; CHRONIC GASTRIC VOLVULUS
HIATUS HERNIA (4)
GASTRIC CARCINOMA WITH MASSIVE HEMORRHAGE; ACUTE MYOCARDIAL INFARCTION
IRRADIATION DUODENITIS (20 YR. POST-IRRADIATION) WITH OBSTRUCTION
TRAUMATIC RUPTURE OF RETROPERITONEAL DUODENUM
DUODENAL ABERRANT PANCREAS

FIGURE 6

COMPLEMENTARY GASTROSTOMY IN ADULTS

Liver, Biliary Tract, Pancreatic Cases (11)

PERIAMPULLARY CARCINOMA (5)
**MAJOR PALLIATIVE OPERATIONS (4)
PANCREATICODUODENECTOMY
*POST-TRAUMATIC HEPATIC RUPTURE (LEFT HEPATIC LOBECTOMY.[6]
*PANCREATIC ASCITES[8]
PANCREATIC PSEUDOCYST WITH BILATERAL PLEURAL EFFUSIONS
PANCREATITIC BILIARY AND SPLENIC VENOUS OBSTRUCTION
PANCREATIC PSEUDOCYST WITH MASSIVE HEMORRHAGE
SUBACUTE PANCREATITIS

*PREVIOUSLY REPORTED
**ONE DEATH

FIGURE 7

COMPLEMENTARY GASTROSTOMY IN ADULTS

Intestinal Cases (13)

**STRANGULATION SMALL-BOWEL OBSTRUCTION
OBTURATION SMALL-BOWEL OBSTRUCTION
OBSTRUCTED CECAL CARCINOMA
CECAL CARCINOMA WITH STERCORAL TRANSVERSE COLON PERFORATION
MULTIPLE INTESTINAL BULLET PERFORATIONS (2)
ILEOCECAL RETICULUM CELL SARCOMA
NEGLECTED GALLSTONE ILEUS
PERFORATED, OBSTRUCTED IRRADIATION ENTERITIS
ACUTE TOXIC MEGACOLON IN ELDERLY FEMALE
RUPTURED ILEOCOLIC ARTERY ANEURYSM
CECAL CARCINOMA IN ELDERLY FEMALE (90 YR.)
COLONIC POLYP

**ONE DEATH

FIGURE 8

COMPLEMENTARY GASTROSTOMY IN ADULTS

Splenic Cases (3)

TRAUMATIC RUPTURE OF SPLEEN AND DIAPHRAGM
SPLENIC PSEUDOCYST DUE TO PANCREATITIS
TRAUMATIC RUPTURE OF SPLEEN

FIGURE 9

COMPLEMENTARY GASTROSTOMY IN ADULTS

Vascular Cases (4)

**AORTIC ANEURYSMECTOMY (3)
**AORTOILIAC BYPASS

**ONE DEATH

FIGURE 10

COMPLEMENTARY GASTROSTOMY

DEATHS	8
WOUND INFECTIONS	4
SUTURE LINE LEAKS	3
WOUND DISRUPTION	1

The Foley balloon is inflated, and traction is applied to the catheter to draw the gastric wall snug against the abdominal wall at the site of catheter penetration. The gastric wall is sutured to the undersurface of the abdominal wall at the gastrostomy site with several sutures, 0 chromic catgut in adults and fine silk in small children and infants. Normally, three sutures are used for this purpose.

The correct position of the Foley balloon is checked by palpation, and if any doubt exists concerning the intraluminal position of the catheter tip, the catheter is irrigated with a syringe.

The catheter is tethered at the skin by a "Chinese thumb trap" suture of 2-0 silk to prevent its dislodgement.

Closure of the abdomen is performed, following which the catheter is further attached by tape and a safety pin to the wound dressing so as to prevent direct traction on the gastrostomy site during the postoperative period by the patient or others.

Pitfalls In Technique

Location of Gastrostomy Site. Consideration must be given to placement of the gastrostomy so that no tension exists on stomach or gastrointestinal suture lines as a result of the gastrostomy. Otherwise, intraperitoneal gastric leakage, following gastrostomy catheter removal, or suture line disruption may occur. Location of the gastrostomy well away from the main abdominal incision to prevent possible contamination of the incision by gastric contents also seems wise.

Perforation of Gastric Wall. If the full thickness of the gastric wall is incised sharply at the proposed site of the gastrostomy catheter, brisk bleeding from the rich submucosal gastric vascular plexus is almost predictable and may persist following operation. Blunt perforation with a hemostat almost never incites significant bleeding, on the other hand.

It is most important to ensure that only the anterior stomach wall is perforated. I know of cases in which catheter tips have been inserted through both gastric walls and placed in the lesser space inadvertently.

Placement of Concentric Pursestring and Gastric Fixation Sutures. The second pursestring suture should be placed enough peripheral to the first pursestring to allow inversion of the site of catheter penetration since, in theory at least, such inversion should contribute to prompt sealing and healing of the gastric stoma following removal of the catheter.

All sutures following inflation of the Foley balloon must be placed to avoid perforating the balloon, which could result in undetected dislodging of the catheter during the postoperative period.

Fine silk sutures are used for fixation of the stomach to the anterior abdominal wall in infants and small children because of the notorious ease with which these little patients prolapse gut loops through abdominal wall stomal sites and because of the greater difficulties in these youngsters with sealing of gastrointestinal defects, regardless of source.

Final Placement and Tethering of Catheter. It is extraordinary with what ease a catheter placed into the gastric lumen will find its way through the pylorus or into the esophagus. A gastrostomy catheter of the Foley balloon type so dislocated may produce distal esophageal or gastric outlet obstruction. It is thus mandatory to confirm the location of the Foley balloon just beneath the site of catheter penetration of the gastric wall and to ensure it after operation.

Postoperative Gastrostomy Management

Immediately following operation the gastrostomy catheter is connected to intermittent suction. If a nasogastric tube has been inserted prior to operation, it is removed. If efficient function of the catheter is doubtful at any time, small amounts of air or saline can be flushed through it to check its patency. A frequent observation is that the volume of gastric fluid content aspirated during the first day or two following operation may be surprisingly small; volumes of aspirate then rise to highly variable quantities. Meanwhile, small sips of water or ice chips are allowed for the patient's oral comfort.

Upon signs of return of normal gastrointestinal function, the gastrostomy catheter is occluded, and the patient is returned to an appropriate oral diet. Frequently, occlusion is gradually accomplished, the catheter being opened at regular intervals to empty the stomach or to allow temporary decompression. If at any time during catheter occlusion the patient becomes nauseated, begins to vomit, or develops abdominal distention, the catheter is opened and reconnected to suction.

The catheter is removed under ordinary circumstances in seven to ten days in adults. In infants, a full ten days is allowed for sealing of the peritoneum around the gastrostomy site before the catheter is removed. Drainage from the gastrostomy site following catheter removal is rare after 24 hours.

In certain cases, the gastrostomy is used to excellent advantage for feeding, although this is a secondary purpose and was not the primary intent of any gastrostomy in the present series.

Discussion

The performance of a gastrostomy requires several minutes but cannot reasonably be considered a real extension of an operation if performed properly in selected cases. No significant extension of the main incision or performance of additional incisions seems justified to accomplish complementary gastrostomy except in highly unusual instances in adults. In newborns, the problem of esophageal atresia demands gastrostomy as a preliminary or complementary procedure for special reasons, and gastrostomy may be the only abdominal operation required.

No single type of case has been considered a "routine" indication for gastrostomy. When one is dealing with difficult problems, several considerations are frequently apparent which make gastrostomy attractive. In my experience, this combination of factors has on many occasions included a history of heavy smoking, chronic pulmonary disease, and a complex abdominal operation in a debilitated or elderly patient. Gastrostomy has frequently accompanied non-resective operations for acid-peptic disease because of the threat of gastric atony following vagotomy, especially if gastric outlet obstruction has been a pre-operative problem. Major abdominal operations in infants seem to be those in which I would feel gastrostomy is most categorically an integral part of the operation.

Certain cases seem poorly suited for gastrostomy. Most true subtotal gastric resections would be included in this group, since fixation of the gastric remnant to the anterior abdominal wall is usually difficult without tension. I have performed gastrostomy in this situation, without abdominal wall fixation, using omentum to seal the gastric stoma around the catheter, without difficulty, but this technique seems more subject to trouble. Patients undergoing portosystemic shunts may develop uncontrollable ascitic fistulas at a gastrostomy site; hence, no such patients are seen in this series. Patients who have required prolonged therapy with cortisone or similar steroids may present special problems in sealing of the peritoneum or healing of the stoma following gastrostomy; they are therefore given especially careful thought before being subjected to gastrostomy.

All infections related to wounds in this group of patients occurred in patients with intra-abdominal sepsis prior to operation except for one. A two-month-old infant with common bile duct atresia drained several cubic centimeters of pus from a subcostal drain site following cholecystoduodenostomy, appendectomy, and gastrostomy. Appendectomy had been performed because of incomplete cecal rotation, the appendix lying in juxtaposition to the cholecystoduodenal anastomisis.

The three instances of suture line leaks were encountered in situations which cannot indict the gastrostomy, because of the anatomy involved. They occurred in the presence of post-irradiation changes, advanced carcinoma, and pancreatitis; death occurred in one patient of this group, an elderly lady with pancreatic carcinoma. No intra-abdominal leakage from the gastrostomy site was encountered in any patient in the study.

One wound disruption occurred among these cases. An infant with suppurative segmental ileitis and generalized peritonitis of undetermined cause suffered evisceration on her seventh post-operative day. The wound disruption was repaired without disturbing the intact gastrostomy; her recovery was subsequently uneventful.

All deaths occurred in the presence of circumstances ordinarily associated with high mortality rates. In none was gastrostomy felt to be implicated in the events leading to death.

As is apparent, the contribution of a single adjuvant maneuver in a group of difficult, nonhomogeneous, surgical problems is impossible to assess in a precise way. To me and to the resident staff involved in the care of these patients, several impressions stand out, apparently related at least in part to the benefits of gastrostomy. First, patients are uniformly grateful to avoid the necessity for post-operative nasogastric intubation; it is no secret how infamous is the nasogastric tube to patients as a hallmark of major abdominal surgery, no matter how vital it may be to post-operative care. Second, gastrostomy greatly simplifies the management of gastric suction for surgeon, resident staff, and nurses alike. Patients do not pull it out; it does not coil in the esophagus, knot in the stomach, slide into the duodenum, or climb into the pharynx with coughing or retching. More importantly, truly serious complications of nasogastric intubation,[10] such as esophageal stricture or post-cricoid abscess, are impossible. Third, the reliability of the gastrostomy tube in preventing abdominal distention is impressive. Finally, one is amazed at the low incidence of problems with clinically important pulmonary atelectasis and pneumonia in these severely ill patients, that incidence being 2.6 per cent in the present series.

Gastrostomy, like every other surgical procedure, must be thoughtfully elected, carefully performed, and appropriately managed. I am very much convinced that, for the surgeon who follows the rules, gastrostomy can be a remarkably valuable option.

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Discussion Of Dr. Strauch's Paper

Dr. John M. Wilson, Norwalk: This paper was obviously prepared with the meticulous detail that Dr. Strauch employs in caring for his patients and in performing his gastrostomies. Too, Dr. Strauch, I suspect, has achieved the statewide record for gastrostomies performed. I suspect that the rest of us are using complementary gastrostomies with less frequency than has been cited in this paper. I believe that all of us could well consider, in the light of this paper, the use of complementary gastrostomies more frequently. As an example of the frequency with which complementary gastrostomies are being performed, I reviewed the records at Norwalk Hospital in the year from September, 1969, to September, 1970, and in 7500 cases, there were only two gastrostomies done of which one was a complementary gastrostomy and one a feeding gastrostomy. I must confess to having done only one gastrostomy in the last ten years.

However, as an example of why I think gastrostomies should be done more frequently, I have had three patients in the last two years who would have benefited by this procedure. I had two patients with vagotomies and drainage procedures who required a later gastrostomy because of markedly delayed gastric emptying after the vagotomy and drainage procedure. One patient did not open the gastric stoma for 2½ months.

I also had one patient who had a cholecystectomy and common duct exploration who required a Levin tube for 36 hours during the post-operative period, who developed, one month later, a 6-inch-long esophageal stricture. The patient had a G.I. series prior to cholecystectomy and had a normal esophagus with a small hiatus hernia at that time.

I think these cases illustrate that, with a little thought on the matter, we could employ this procedure more often. If we do elect to perform this procedure more often, I think the key point is meticulous attention to the details of the operative procedure.

Perhaps the most recent famous patient to have a complementary gastrostomy in the past few years is former President Johnson who had one done after his cholecystectomy and renal stone extraction. Apparently President Johnson did not want to be photographed with a Levin tube down his nose. He developed an incisional hernia at the gastrostomy site which required a later operative repair. I think this illustrates the need for meticulous attention to the details of the operative procedure to avoid the complications that may occur when this procedure is used.

Dr. William T. Livingston, New Britain: It is a pleasure to comment on a paper with which one definitely agrees. Certainly this is the case with Dr. Strauch's paper, which I found most interesting, and I certainly strongly support his contention that complementary gastrostomy is a useful tool.

In New Britain, in the past two years, we have done 32 gastrostomies, some 20 of which were complementary. The other 12 were for feeding purposes. Of the 32 none have had any complications. I have done a fair number myself, not nearly as many as Dr. Strauch perhaps, but I personally have had no complications from this procedure. I recently saw a patient in whom a complementary gastrostomy was done in conjunction with the repair of a hiatal hernia in a neighboring institution. The placement of gastrostomy site on the abdominal wall was unfortunately too close to the costal margin, and consequently there was a persistent fistula; but even this one closed up with simple local measures.

Certainly the reason for doing complementary gastrostomy is quite clear. You are attempting to avoid the pulmonary complications that we all see resulting from the use of a Levin tube. I consider the Levin tube in certain situations a rather lethal weapon, and it should be avoided if possible. Its complications come from pulmonary complications and from the tube itself resting in the esophagus. My personal criteria for using this procedure are any patient who is very young, or very old, or who has serious pulmonary disease, who is going to need post-operative nasogastric suction, provided the complementary gastrostomy can be done without making a new incision, as Dr. Strauch pointed out.

I would take one issue with him. I don't like the Foley catheter as the gastrostomy tube for two reasons. One, I have seen the balloon that would fail to deflate when you wanted it to, and this is a little bit awkward because you now have to puncture it in some fashion and this involves a blind stabbing or a little sweating; or else you force it out through the abdominal wall, which can be done, but you then worry that you might disrupt your gastrostomy sinus. Secondly, I have seen Foley catheters which failed to drain by virtue of distending the balloon. The blowing up of the balloon simply collapses the internal lumen, and there is no drainage pathway. For these two reasons I prefer to use the old fashioned mushroom catheter which certainly works very well.

Dr. Strauch: I thank my discussants for their generous supportive comments and also for their critical ones. I think the choice of tube for gastrostomy is a matter of personal preference. I certainly agree with Dr. Livingston that the Foley catheter, if it is not properly functional, may be a problem. We have not had difficulties with it.

It may be of interest to give you some idea about the incidence of gastrostomies in Stamford, Connecticut. I asked the Record Room to pull out all gastrostomies performed by all members of the surgical staff at both hospitals in Stamford, except for mine, for any reason—feeding gastrostomies or complementary gastrostomies—for the past five years. The entire remainder of the surgical staff in Stamford had done 41 gastrostomies while I had done 64. You can draw your own conclusions.

For as the subtlety and variety of the subject afford many opportunities for cure so likewise a great facility for error.—Frances Bacon

Connecticut Medicine

Editorials

Studies In Genetic Engineering

The problems of inserting specific genes into human cells which has intrigued molecular geneticists have now matured into hard experimental work. It now appears that animal viruses, bacterial viruses and cell fusion techniques are all capable of introducing new functional genes into mammalian cells although many of the fundamental genetic and regulatory processes in mammalian cells still remain unknown.

As far as bacteria are concerned, geneticists can often produce a specific mutation in any of a large number of genes in Escherichia coli. He can delete genes or add new ones from outside the cell and can then regulate the expression of genetic traits inside the cell. Now we find Munyon and his group[1] at Roswell Park Memorial Institute in Buffalo successfully infected a mutant type L cell from mouse tissue culture that lacked the enzyme thymidine kinase with an animal virus herpes simplex. They had to destroy first the virus's ability to kill the cell by irradiating the virus with ultraviolet light. Herpes virus normally induces a thymidine kinase activity during infection before it kills. In this experiment 0.1 percent of the infected L cells were transformed by irradicated virus into stable cells that had thymidine kinase activity and were maintained for eight months in culture.

The results are consistent with the idea that the herpes simplex virus introduces a gene for thymidine kinase into the L cell that was deficient in it and that this gene had been maintained and replicated by the cells.[2]

We have already seen in these pages that Merrill and his group have shown that a bacteriophage is capable of introducing a selected gene into human cells. He worked with the bacterial virus lambda phage, one of the transducing phages of E. coli. Transducing phages have been the most useful genetic tools available to molecular biologists because they can selectively introduce new functional genes into bacteria. Merrill treated a human fibroblast from a case of galactosemia which lacked the enzyme to metabolize galactose. The cultured fibroblasts were treated with lambda phage which carries a set of gene that codes for the enzyme which converts galactose to glucose and controls their synthesis. The fibroblasts actually were transformed by lambda phage and became capable of metabolizing galactose. The experiments performed by Merril have thus shown that lambda DNA can enter human cells and once there at least some of its genes can be replicated, transcribed and translated.

Viruses are not the only means of introducing new genes into mammalian cells, however. Henry Harris and his group at Oxford in England have now shown that cell fusion can also be used to insert a functional gene from chicken cells into mouse tissue culture cells. If two cells are fused, or if another's nucleus is introduced into a cell, the dividing time of the resulting multi-nuclear cell is primarily determined by the nucleus that is closest to division. The other nucleus may be forced to divide before it is ready and their chromosomes usually undergo a "premature condensation" which results in their fragmentation and pulverization. The Harris group fused chick red blood cells whose nucleus carries the gene for chick inosinic acid pyrophosphorylase with mouse fibroblasts A_9 cells which are a mutant line of mouse L cells deficient in this enzyme.

During cell division the nuclear membrane in these hybrid cells disappears and the chick's chromosomes undergo pulverization. Although only mouse nuclei appeared in the daughter cells after mitosis, some of the daughter cells had gained the ability to synthesize chick inosinic acid pyrophosphorylase. After more than 100 generations in culture, 20 percent of these transformed hybrid cells lost their ability to make this enzyme. Obviously, it was not as stable as genetically stable normal mouse cells for this enzyme.

A number of laboratories are already extending these gene transfer techniques. Aposhian and his group is now studying the genetic properties of polyoma pseudovirus in mice. They are also attempting to produce polyoma pseudovirus containing the gene for human thymidine kinase. Merrill has infected whole animals with transducing lambda phage in order to determine whether any new traits gained by the animals from the genes that are transported by the phage can be inherited from one generation to the next. The ability to transfer small segments of DNA from one cell to another gives molecular geneticists the opportunity to map locations of genes within mammalian chromosomes. In turn, understanding the method by which genes are organized into functional units within the chromosome may reveal how the regulation of gene expression takes place. This regulation may play an important role in the differentiation of animal cells.

Current developments certainly do not yet add up to "genetic engineering" but there now exists very strong evidence with a number of different techniques that experimenters can transfer genes between and insert them into mammalian cells, a development which opens to experiment many questions about gene function in animals and in humans.

Now that a few of the basic tools of molecular genetics have been extended to animal cells more than a few biologists share Aposhian's concern that science "will give us gene therapy before society is prepared for it."—L.H.N.

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Fifty Years Of Tuberculosis

During much of the first half of this century the sanatorium treatment of tuberculosis demanded a high price for recovery from the patient in the form of courage, discipline and perseverance. A surprisingly high number succeeded when aided in 1930-1945 by collapse therapy. At that time, the disease was prevalent in all segments of the population but then as now there were great reservoirs in the poverty-stricken, illiterate and unmotivated which had yet to be exposed by case finding.

The period from 1945 to 1955 led to great success in control and treatment and even raised hopes of eradicating the disease. This made inevitable the final decline and dissolution of the sanatorium era. However, the skillful physicians of the sanatorium declined also and this left a knowledge void. This 10 year period saw three great advances; extensive use of miniature chest x-ray; development of the surgical technics making lung resection for pulmonary tuberculosis feasible and of course most important, the discovery and use of chemotherapeutic drugs, streptomycin and P.A.S. Over the last 15 years the combination of intensive case finding and vastly improved therapy has yielded results entirely beyond the grasp of the previous era. Multiple drug therapy for as long as 2 years has radically changed treatment methods. Thus exercise has replaced rest except in early toxic cases. Surgery is seldom used and treatment is mostly at home rather than in hospital.[1]

Beside streptomycin, I.N.H. and P.A.S., a number of drugs have been developed of which the newer ones ethambutol and especially rifampin may prove to be the most effective yet. Figures from the Dominion Bureau of Statistics which probably reflect accurately the condition in this country show the following remarkable changes. Since 1945 mortality rates for tuberculosis in Canada[2] have dropped from 50 to less than 2 per 100,000 and new case rates from 118 to 18 per 100,000. A plateau, however, has been reached in the last 5 years. Clearly sanatorium beds had to be converted to other uses. At the same time the tuberculosis patient has returned to the mainstream of general medicine and every physician now needs to be well informed. The need is great for teaching tuberculosis which now begins in the general hospital with early diagnosis, immediate institution of therapy, single room isolation and masking of the infective patient when off the wards.

The danger of infection rests mainly with an unidentified case. The staff needs to be routinely examined, Mantoux-tested and given BCG or chemoprophylaxis as indicated. After the diagnosis has been made patients should be transferred to appropriate chest units for continuing treatment which still require the knowledge and experience of practicing chest specialists who are acquainted with the problem of drug resistance, toxicity and allergy. Preferably such units should be in medical centers allowing ready consultation in associated diseases and also contributing to undergraduate and graduate training.

It is of interest that two-thirds of new cases are still not discovered until they are advanced and infective and often not before a good many days stay in a general hospital. With few exceptions, patients with new disease are from low socio-economic groups. They do not stay on treatment either in hospital or at home as well as patients in the previous era.

The ability of the bacillus to remain inactive and tolerated by tissues for years, yet ultimately to cause active disease is one of the greatest obstacles to control and final eradication of tuberculosis. How best to combat this imponderable host-bacillus relationship is our greatest problem. One approach is to prevent it by the use of BCG and Frappier[3] reports the considerable reduction in morbidity and mortality attending the use of this vaccine in certain age groups in Canada. BCG has not been widely used in areas of Canada where the general incidence of infections is low. Its value has been accepted in high incidence groups such as Indians and Eskimos and it is being strongly recommended for groups with unusual exposure such as persons working in hospital or in social and welfare services.

Chemoprophylaxis is another approach to the same problem. Its use is based on the assumption that a person with a naturally occurring positive tuberculosis reaction is more likely to have a reactivation of the disease than to be protected by his acquired resistance. On this basis all those with Mantoux reactions of over 10 mm. to 5T.U. of P.P.D. are recommended for a 1 year course of INH. Of this group, prime candidates are recent converters and old patients with inadequate or no previous chemotherapy. Many of the inactive cases of tuberculosis fall into this class.

Even though the sanitorium has given way to the general hospital for inpatient treatment of tuberculosis, existing public agencies must be continued and indeed strengthened. These include notification and registry, X-ray and tuberculosis surveys, diagnostic follow-up and outpatient chemotherapy clinics as well as the supervision of home chemotherapy especially in outlying areas. Without them the control of tuberculosis would indeed disintegrate. The report by Kincaid[4] on the containment of a tuberculosis outbreak attests to the effective functioning of such agencies.

One of the most difficult problems today is the high incidence of patients who are delinquent in taking drugs at home. Indeed outpatient chemotherapy is the weakest link in the treatment chain and its supervision will require a far greater expenditure of time and money than is now expended. Fifty years ago, Sir William Osler taught his students that tuberculosis was a social disease with medical aspects. This is even truer today and it might well be that final eradication will not be advanced until poverty and even privation have been removed from our society.

Medicine, of course, cannot await for such a utopia. However, any significant further advances will depend on how well tuberculosis is absorbed into the mainstream of medicine. For this, sound backing will be of prime importance. —L.H.N.

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Smoking: Successes And Failures

The Royal College of Physicians of London and WHO held a conference on how to control the dangers of smoking.[1] One promising note was struck but even this was in an area that is bound to be controversial. Some say it is foolish to talk of a safe or even a less dangerous cigarette because such a limited effect could be self-defeating. It might for example undermine the work of school programs when a child is taught that smoking is dangerous and then returns home to parents who are smoking a carefully chosen product—as "safe." A practical objection was also raised to a "safe" cigarette. By lowering the tar and nicotine content of cigarettes, how can we be sure that the smoker will not puff more vigorously to compensate for the nicotine loss and so actually inhale more tar products.

In the U.S. and Germany from 1956 to 1968 the average nicotine content of the best selling brands almost halved to about 13 mg. and the tar content fell by a similar proportion to 20-25 mg. In Britain, the change has been less spectacular. Dr. E. L. Wynder of the National Cancer Institute reported that we had gone a long way towards identifying the harmful products in tobacco smoke, at least as far as lung cancer is concerned. The solid phase of smoke (particulate) contain 12 well-known polycyclic aromatic hydrocarbons and tumor promoters and accelerators. The gas phase contains 3 nitroso derivatives known to be carcinogenic.

The precursors of the polycyclic hydrocarbons are terpenes and phytosterols in the wax surfaces of tobacco leaves. Accordingly, using more stem tobacco might be a step toward a less dangerous cigarette. Smoke from reconstituted tobacco with a high cellulose content also has a lower tumorigenic capacity. These studies were done on animals but research is planned on the epidemiology of tumors based on the brand smoked i.e. taking into account the composition of the tobacco. Curiously no mention was made about polonium 210 present in tobacco leaves and being radioactive has been shown to be trapped in the respiratory mucosa and closely correlated with tumorigenesis in smokers.

The position is less clear for smoking and heart and respiratory tract disease. In atherosclerosis nicotine and also carbon monoxide play a causative role. Chemical research has identified also in tobacco smoke phenols, aldehydes and hydrocyanide which can destroy the defence characteristics of the respiratory system.

In many countries the longest experience with smoking control has been in smokers clinics and school publicity programs with not too much success. In fact, the conference was told that in many countries smoking by children is on the increase. The emphasis in some countries in youth oriented health education is not so much on far distant hazards but on present fitness, notably in athletic success which many boys rate highly.

The simplest explanation of smoking among school children is that it is a way of attaining peer respect. Also and paradoxically, the child who smokes is copying an adult habit yet at the same time, defying adult authority. In Germany an experiment is being carried out having direct participation of the young in carrying out the program. It appears, however, that among poorer groups and poor nations the smoking habit is proven more recalcitrant. In fact, manufacturers are seeking to increase sales in developing countries where populations are quite vulnerable. It was further pointed out that governments which are responsible for the health of citizens seem happy to raise money from the sale of products known to harm health.

On research there are many gaps but one of the greatest is that we do not even know why people smoke. The psycho-pharmacological aspects of habituation has received almost no study and even if prospects along these lines were to be begun immediately it would be years before correct anti-smoking programs could be available. Somehow, clinical research on smoking was held by the research community to be unglamorous and somehow not suitable for serious science. It appears no one applies for grants for work of this kind.

Summarizing the conference, it appears that anti-smoking persuasion is having some success with adults but mostly in the middle classes but campaigns aimed at children have not yet had much measurable effect. By reducing the tar and nicotine content of cigarettes and by giving continuous publicity to these levels, those who cannot stop smoking will at least as far as lung cancer is concerned, run less of a risk, how much less is not known. Governments must now step in and legislate for this publicity and proceed towards a ban to all advertising of tobacco

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*Data compiled from reports of 14 investigators. **Diagnosis was confirmed by cultural identification of *N. gonorrhoeae* on Thayer-Martin media in all patients. Criteria for cure: negative culture after at least 2 days post-treatment in males and at least 7 days post-treatment in females. Any positive culture obtained post-treatment was considered evidence of treatment failure even though the follow-up period might have been less than the periods cited above under "criteria for cure" except when the investigator determined that reinfection through additional sexual contacts was likely. Such cases were judged to be reinfections rather than relapses or failures. These cases were regarded as non-evaluatable and were not included. JA72 1848-6

globin; hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

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products. Voluntary organizations need and deserve support. It is hoped they would proceed with enthusiasm and imagination tempered with tolerance and patience.—L.H.N.

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An Index For Measuring Health

We are spending 6.7 percent of our GNP in the study, prevention and treatment of ill health and yet we have no method of measuring the patient's health before and after treatment. For a variety of reasons it would be beneficial if we had a reliable health index which measures health and allows severity of disease, efficiency of treatment and even costs of all these to be compared.

Medical care of course includes frequent evaluations of the patient's health but the measurement is practical or relative and is expressed in such terms as "now fit for light duty" or "better than yesterday." Such an assessment to be sure serves the doctor fairly well but they do not lend themselves to numerical representation. Indeed, without first having a suitable definition of health upon which to base the score numerical representation is impossible.

WHO defines health as a state of physical, mental and social well being, and this definition has been used as a basis for some early trials. It is a reasonable definition but it does not encourage precise scoring. Accordingly Grogono examined the activities and aspects which together comprise the pattern of daily life. Finally they produced a list of ten items which are comprehensive and yet without redundancy.

One is work. The score is to be awarded on the basis of ability to do tasks associated with every day life. If normal the score is 1. If impaired or reduced the score is ½. In unable to work the score is 0. A second is hobbies and recreation. If they are normal again the score is 1. If impaired or reduced the score is ½. If prevented from pursuing them the score is 0.

The third item is physical suffering. If the patient is free from malaise, pain or suffering he scores 1. If partially free he scores ½. If he actually has malaise, pain and suffering his score on this item is again 0. The fourth item is mental suffering. If free of them he scores 1. If he suffers from worry or unhappiness his score is 0. The fifth item is communication. The scoring is whether the person is normal, impaired or incapacitated. Language barriers alone should not produce a reduced score.

The sixth item deals with satisfactory sleep, whether it is normal, impaired or whether the person is sleepless. The seventh item is whether the person is independent or whether he needs assistance for the acts of daily living, working,

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dressing, moving. This score should be reduced if the assistance of others is required on medical grounds or on medical advice. Item eight is whether the patient enjoys his food. His score will be reduced if he dislikes it.

The ninth item is whether defecation or urination is normal. If there is a major abnormality of either of these functions the score is 0. The final item is whether the patient's state of health has altered his sex life. Infants, children and the celebate would normally score 1, even during disease since no deprivation occurs. If deprivation occurs in others then the score is 0. If no deprivation the score is 1. The score of a normal person is thus 1, ill health causing a reduced score and extreme ill health scoring 0. This approach corresponds to a definition of health as "no impairment in the aspects of life listed."

These 10 factors were then used as the basis for scoring a patient's health with each factor considered in the same way. The ten questions were presented as a list with space for recording details of the patient and observer and room for several scores to be made. Twenty observers made 180 assessments on twenty-seven patients. The variation between observers was slight. Many patients were seen more than once. Such as a woman with asthma who started with a score of 0.4 which rose to 0.9 when she improved. Heart failure scored .35 but on treatment rose to .75. Myocardial infarction scored .65 and could, of course, rise to 1 on satisfactory recovery.

The health index can be used in a variety of ways. One as a weighting factor giving a value in health terms to any period of time and expressed in life years. One year in full health is one life year. One year with a health index of .5 is ½ life year. Benefit from treatment can thus be expressed as health years or parts of a health year gained to the patient as a result of the measures carried out. In the same way the impact of a disease can be expressed as health years lost to an individual or to the community.

If the health index is combined with satisfactory measurements of cost it should be possible to apply cost benefit analysis to health. Hitherto the appropriate information about cost has not been available.—L.H.N.

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Infirmities In The Aged: Some Consequences Of Medical Progress

Certain desired and perfected medical technologies have already had some dehumanizing consequences. Improved methods of resuscitation have made possible heroic efforts to save the severely ill or injured. Often such efforts are only partly successful. They may succeed in salvaging the individuals with severe brain damage, capable of only less than human vegetating existence. Such patients have been denied a death with dignity. We struggle to keep them alive by treating for example a complicating pneumonia when we know full well as Osler once put it that pneumonia is the best friend of the aged.

Families are forced to suffer seeing their loved ones so reduced and are made to bear burdens of a protracted death watch. Even the ordinary methods of treating disease and prolonging life have impoverished the context in which men die. Fewer and fewer people die in the family's surroundings of home in the company of family and friends. At that time of life when there is perhaps the greatest need for human warmth and comfort the dying patient is kept company by cardiac pacemakers, defibrillators, respirators, aspirators, oxygenators, catheters and of course the irrepressible intravenous drip.

But the loneliness is not confined to the dying patient in the hospital bed. Consider the increasing number of old people who are still alive, thanks to medical progress. As a group the elderly are the most alienated members of our society. Not yet ready for the world of the dead, not deemed fit for the world of the living, they are shunted aside. More and more of them spend the extra years medicine has given them in Homes for Senior Citizens, in chronic hospitals, nursing homes, waiting for the end. We have learned how to increase their years. But we have not learned how to help them enjoy their days. An especial terror is an alert mind trapped in a failing body.

At the 20th Annual Convention of the Kansas Nursing Home Association in Topeka, Dr. W. B. Tarnower spoke of how much one can learn about the problem of the aged by looking into a home. It may look beautiful on the outside but when one steps in he may feel an immediate cultural shock. He steps into another world where people are old, infirm and often cut off from others because of difficulty of seeing and hearing.

One is reassured to see the staff getting the daily work done feeding and dressing patients, helping the incontinent ones and assisting patients to the front desk to watch the comings and going of people. Sometimes members of the staff will try to help the old people to cope with emotional problems that range from chronic depression to aimless wandering. But one sees with mixed feelings half-dead people who are being kept alive by medical science and doctors, wondering if that is always the kind or right thing to do. A number of patients are obviously unable to derive any significant pleasure from life. Some of them would choose to die if death were free for the asking.

Many of the inmates of nursing homes resent the fact that they are in constant contact with people almost all of whom are old, and it bothers them greatly that they must observe the physical and mental deterioration of those around them. They may envy those who are in fair health and the more handicapped feel themselves growing older and more dependent on others. They may be tormented by irrational thoughts and react in an irrational manner. Thus anxieties increase as they must face anything new, technical or legal, that emphasizes the strangeness of the environment they cannot control and this may make them angry or negative in their attitude. Some patients may fear that there will be reprisals if they complain and that the little they are given will be taken away from them. They worry that if they fuss too much they may be shipped to another nursing home or a state hospital.

What can one do in the face of such problems? As physicians we have the privilege of trying to ameliorate many of the problems of the aged, provided we are willing to become involved and are willing to listen. By listening we may not only help to relieve the complaints of the aged but may simultaneously elevate the patient to the status of a worthwhile and respected human being. The stress largely by the aged on physical contact should not be minimized. A pat on the shoulder, a mere touching of hands will often transform a reluctant or depressed individual into somebody who suddenly becomes responsive and is eager to unfold the problem which he previously kept subdued. He realizes he is now telling his story to an indi-

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vidual who is sufficiently concerned actually to make contact with him. Experienced physicians know that physical contact with a patient is a significant factor in the development of an excellent physician-patient relationship.

Further to learn what underlies an old person's behavior, some nursing homes employ social workers and mental health workers to discuss their problems with the families of patients. This approach can lead to a deeper understanding and an extra measure of happiness for both patients and staff. This can help the family also to be more kind and patient with their old relatives. Stress must be made on the psychological support so urgently required by the aged. In no other field of medicine is the practice of the art of medicine so important.

Let us make sure that custodial care is not the equivalent of the inscription Dante read over the Gates of Hell "Abadon hope all ye who enter here."

Instead let us strive to realize what Seneca said "the gradually declining years are among the sweetest in a man's life and I maintain that even when they have obtained the extreme limit they have their pleasures still."—L.H.N.

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Some Advances In Biomedical Science With Social And Moral Implications

Recent advances in biology and medicine suggest that we may be rapidly acquiring the power to modify and control the capacities and activities of men by direct intervention and manipulation of their bodies and minds. The power for human engineering is coming and it will probably have profound social consequences. When they come, the hope of course is that we can harness the new technology of man for the betterment of mankind. The advances are fruits of a large humane project dedicated to the conquest of disease and the relief of human suffering. The biologist and physician are seen as the well wishers and benefactors of mankind.

Some of the advances in biomedical science can be grouped under three major categories: the control of life and death is advancing rapidly. Medical triumphs have greatly increased the average life expectancy. Research into aging holds forth the promise of increasing not just the average but also the maximum life expectancy. Aging is now thought to be a genetically controlled process distinct from disease and one that can be manipulated and altered by diet, drugs and ultimately by eugenics. Extrapolating from animal studies, some scientists have suggested that a decrease in the rate of aging might also be achieved simply by effecting a very small decrease in body temperature. According to some estimates, by the year 2,000 it may be technically possible to add 20-40 useful years to the period of middle-life.[1]

Control of death is occurring alongside of controlling birth. New techniques are appearing for lowering fertility including chemical agents for inducing abortions. But they are also developing techniques to promote fertility. The first successful laboratory fertilization of a human egg by human sperm was reported by Edwards in 1969. In 1970 the British scientists learned how to grow human embryos in the laboratory at least up to the blastocyst stage (1 week). We soon expect to hear about the next stage of the successful re-implantation of such an embryo into a woman previously infertile because of oviduct disease.

The development of an artificial placenta now under investigation will make possible full laboratory control of fertilization and gestation. In addition sophisticated biochemical and cytological techniques of monitoring the "quality" of the fetus have been and are being developed and used. These developments not only give us more power over the generations of human life but make it possible to manipulate and to modify the quality of the human material.

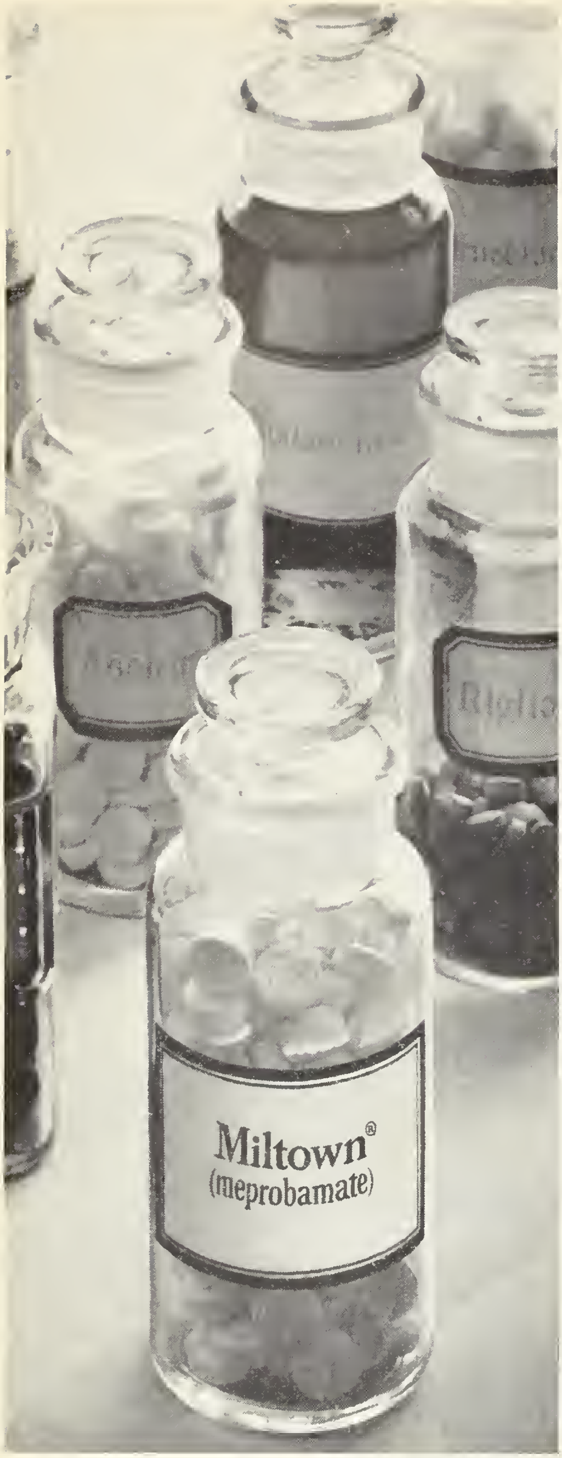
This brings us to the problem of controlling human potentialities. Genetic engineering when fully developed will yield two powers not shared by ordinary medical practice. Medicine treats existing individuals and seeks to correct deviations from a norm of health. By contrast, genetic engineering will be able to make changes that can be transmitted to succeeding generations and will be able to create new capacities and hence to establish new norms of health fitness.

At present, one of the major interests in genetic manipulation is strictly medical: to develop treatment for individuals with inherited disease. Genetic disease is prevalent and increasing, thanks partly to medical advances that enable those affected individuals to survive and perpetuate the mutant genes. The hope is that normal copies of the appropriate gene obtained biologically or synthesized chemically can be introduced into defective individuals to correct their deficiencies. There is some doubt about such therapeutic uses of genetic technology because the same end could probably be achieved by eugenic means.

Far less remote than the above possibilities are the technologies that could serve Eugenic ends. Artificial insemination to improve the genetic pool with selective donors[2] has been possible for several years because of the perfection of methods of long-term storage of human spermatozoa. New methods to select ova as well complete the circle. But a far more suitable technique for eugenic purposes will soon be upon us, namely, nuclear transplantation or cloning.

By passing the lottery of sexual recombination, nuclear transplantation permits the asexual reproduction or copying of an already developed individual. The nucleus of a mature but unfertilized egg is replaced by the nucleus obtained from a "specialized" cell of an adult organism or embryo, for example, a cell from the intestine or skin. The egg with its transplanted nucleus now develops as if it had been fertilized and barring complications will give rise to a normal adult organism. Since almost all of the hereditary material (DNA) of a cell is contained within its nucleus, the renucleated egg and the individual into which it develops are genetically identical to the adult organism that was the source of the donor nucleus. Cloning could be used to produce unlimited numbers of sets of genetically identical individuals each set derived from a single parent. Cloning has been successful in amphibians and is now being tried in mice. Its extension to man merely requires the solution of certain technical problems.

Other less direct means for influencing the gene pool are already available as our ability increases to identify and diagnosis genetic diseases. Genetic counselors can now detect biochemically and cytologically a variety of severe genetic defects, for example, Mongolism and Tay-Sachs disease while the fetus is still in utero. Since treatments are at present unavailable, diagnosis is often followed by abortion of the affected fetus. In the future more sensitive tests will also permit the detection of heterozygote carriers, the unaffected individuals who carry but a single dose of a deleterious gene.



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There are also in the offing attempts at control of human achievement. Heredity determines the material upon which experience and education determine the form. The limits of many capacities and powers of an individual are indeed genetically determined while the nurturing and perfection of these capacities depend upon other influences. Neurological and psychological manipulation hold forth the promise of controlling the development of human capacities particularly those long considered most distinctively human: speech, thought, choice, emotion, memory and imagination.

These techniques are now in a rather primitive state because we understand so little about the brain and mind. But it is time we began to think of the moral aspects involved on the use and possible abuse of all these powers that are already on the horizon for man.—L.H.N.

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Psychiatric Teaching In The Physician's Office: II

The psychiatrist found that he could help the physician pick up points to make it profitable to see what he was doing and where the difficulty was. For example the physician was shown the occasions when he prematurely closed the transaction with the patient or impeded the flow of the patient's information giving, by asking too many questions as well as by failure to see the broad scope of his medical task. Accordingly the following guidelines evolved.

First was the need to observe the total patient. If the physician relied on the patient's tendency to divide their troubles into physical and other complaints then socio-economic and psychological factors would often escape scrutiny. It is only when all these areas are integrated that it is possible to understand more thoroughly the patient's problem.

An example was that of the "strong man." This was an unusually strong, sturdy-looking man in his late 50's who presented two complaints and a career change as the focus of his visit. The first was a contact dermatitis with a history of annual recurrences. The second was paresthesia of the left hand which a dentist in an offhand way had said might represent a heart attack. As part of his "verbal behavior" the patient also spoke about returning to his "trade" after some years of driving and selling. His original trade was that of a steam fitter and he felt he had to get back in shape in order to do this work. His appearance was that of a man 10 years or more past his actual age. The doctor's behavior was striking in that he dealt with each of the prescribed complaints separately. In the corridor the psychiatrist pointed out to the physician that he was dealing with each of the patient's complaints separately. He was assisted to realize that the complaints needed to be integrated into a total view which included an understanding of the patient's struggle against time, weakness and aging even though he was a relatively intact person.

The second principle was that it is necessary to keep in mind not only the obvious details. One must also strive for an integrated view, i.e. to learn to include all data. Every behavior of the patient, his greetings, banter, small talk, seeming irrelevancies, body movements, guestures, can be assumed to be a communication to the doctor, a communication relevant in some way to the current health problem. It might become useful to extend the duration of history taking as well as pay attention to clues which will be missed for lack of acumen but also because of habituation to traditional medical procedure. It is seldom that the problem in any case can be grasped in toto in one visit. However, it is likely that the patient will benefit in some way from the doctors effort in this kind of grasp.

A third guiding principle to emerge was that careful attention be given to the psychopathology of life eras as a guide to the totality of the patient and his complaint. One example was the pubescent boy brought in by his father not mother for a minor complaint present a long time without exacerbation when it was his era in life that needed help.

A fourth guiding principle was the necessity of quick recognition of major but hidden syndromes especially that of depression. A case in point was that of a patient just over a myocardial infarct. He had no real complaints, but he seemed uncomfortable, and sweaty. His facial expression and his sitting at the end of his seat added to this impression. This visit ended. The

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psychiatrist pointed out to the physician the splitting of verbal and somatic data leading to the impression that the patient was heavily involved in denying fears of recurrence of the illness and death. The suggestion was made to have the patient return so that the physician can take note of the splitting with the patient in an open manner thus reducing the denial and making possible a more rational and relieving doctor-patient relationship.

It became clear that the presence of the psychiatrist-teacher mobilized the physician's ability to broaden his scope of practice. This in turn gave him a sense of mastery, control and excellence which enhanced his self-esteem. There was understandably also concurrent improvement in the doctor-patient relationship which was rewarding to the doctor's efforts. Plainly these dynamic formulations need to be more closely investigated and if they are even in part correct, they may explain both why the teaching is worthwhile and how its effectiveness can be even further improved.

It is important that sufficient emphasis and support be given to the learner in his capacity for observation and in proper timing and summarization of clinical material. In his office, his learning has to do with the capacity to learn something new about the patient but not to react to it immediately. The capacity for delay in application of newly discovered clinical material is hard to achieve. Most physicians are hampered in this regard by their urge to heal. He must, however, learn to consider carefully the patient's rate of tolerance for insight. In psychotherapy it is a common observation that too early interpretation slows the treatment by increasing the resistance to insight.

This one-to-one teaching method allows the psychiatrist to step out of customary isolation with his patient and into a position where he can display and communicate his clinical skill directly to the non-psychiatrist. Unfortunately, approximately 2-3 years attendance is needed for a physician to develop a workable understanding in psychological medicine. With 10 student physicians per psychiatrist over a 3 year period, each student invests about 150 hours while one psychiatrist devotes an average of 15 hours per student physician. It will be a slow process of converting physicians to an understanding of psychological medicine but it will achieve infinitely more than attending seminars.

Passive learning is not a good replacement for active participation as a method of learning.

The preceptorship model of medical education is an antecedent to our present way of teaching. Zabarenko and his colleagues have reintroduced it in this experiment where a psychoanalytically trained psychiatrist served as preceptor for a family physician in the physician's own office. —L.H.N.

Reference

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Some Things That Are Happening In British Medical Practice

Britain is losing 400 home trained doctors a year. Most of the number emigrate to the U.S., Canada and Australia. The prime motivation has been recorded as a search for a degree of professional satisfaction that is impossible under socialized medicine. What this means is two fold. First is that four of British Medical Schools are in effect turning out doctors that will practice in other countries. Second, that the resulting shortage has to be overcome in part by immigrant doctors mainly from underdeveloped countries. In fact, overseas doctors now fill no fewer than 52 percent of all junior posts in Britain's hospitals. In the city of Manchester the percentage has reached an all time high of 73 percent and of the country's entire doctor population more than 25 percent are foreigners.

Dr. Paul Good, President of Saskatchewan's Medical Association reports a somewhat similar situation since socialized medicine was fastened on the medical profession in that Canadian Province. Of the original 900 physicians in that province 800 have emigrated to other areas leaving the practice to newcomers and a few who found it too difficult to emigrate.

In Britain often the jobs allocated to immigrant doctors are in the least attractive departments in the worst hospitals. Ten years ago Lord Taylor told the House of Lords "the foreign born doctors are there to provide pairs of hands in the rottenest worst hospitals in the country because there is nobody else to do it—there is no nonsense about teaching in these places.—We are putting them in thoroughly unsatisfactory hospitals where the conditions are often so bad that you cannot expect Englishmen to work there."

Treatment of overseas doctors are no better today and the British medical profession is seriously worried about the tensions generated by the presence of such a large overseas element. Indian doctors who form a high proportion of the total number of foreign born doctors are so worried about the situation that they want to form the Indian Medical Association which so far has been a purely social organization into a pressure group to put their point of view. Dr. Mohan Kalaria, an Indian consultant geriatrician who has been in England for more than 20 years says "The last thing we want is to get involved in politics but you can't expect doctors to work in dumps forever. . .'

Even with the help of overseas doctors, the plight of hospital casualty departments is becoming desparate. Monday, one of the worst days of the year for road accidents, thirteen London hospitals had to close their casualty departments because not enough doctors could be found to keep them open. A similar situation was reported in hospitals outside London. The BMA and RMC are expressing increasing concern about the steadily worsening situation.

Doctors at a large midland hospital are protesting against an instruction to pharmacists to alter prescriptions and substitute cheaper drugs. The order was issued by the Medical Staff Committee of a Birmingham hospital group which administers thirteen hospitals, because there is a "growing concern" over increasing drug expenditures in the group. The BMA has made it clear that doctors must be consulted first before cheaper drugs are given and a spokesman for the association has said "if the contention is to dispense something different without consulting the prescriber, doctors will take great exception. We appreciate the concern over costs but a doctor must retain full responsibility for the treatment he gives his patient." Pharmacists employed in the group are also protesting against being turned into "watchdogs" over their doctor colleagues.

Apparently when the government becomes involved in organized medicine and in the payment of accounts, its only interest is in costs. The quality of care that is given is really of secondary importance to them.—L.H.N.

Reference

1. Hobson, J.: Life with the N.H.S. Private Practice 3: 12, November 1971.

New Prospects For Reproductive Biology

Changes in reproductive biology are almost certainly in the offing. One comes from the laboratory of Dr. R. G. Edwards and his colleagues at Cambridge who are working on the project of fertilizing human eggs in vitro and then reimplanting them in-utero at an early stage of their growth. This is inevitably a controversial subject with a promise to some and a threat to others that such research will make a revolution in social as well as scientific thinking. This was reflected in the last few weeks by attacks by two Nobel Laureates, Dr. Francis Watson and Dr. Max Perutz. Although Edwards' technique may be able to overcome some forms of infertility Watson and Perutz argue that it involves very great and quite unjustifiable risks of producing a defective embryo.

Whether or not what seems likely to develop into a campaign to stop such work is successful, other changes in reproductive biology are almost at hand. It will not be surprising for example if recent developments in distinguishing sperm carrying a Y chromosome from those bearing an X chromosome, should lead to a ready technique for separating sperm according to whether they determine a male or a female child. Coupled with the use of artificial insemination this finding implies that it may become possible to choose the sex of progeny.

Not every one will agree on the value of advances of such a nature, but research on embryogenesis itself has in general produced results that can be universally applauded. Immunological studies of fetal-maternal relationships for example have already proven their use in Rh positive babies to survive in rhesus negative mothers. Indeed, histocompatibility studies on fetal development may lead to a better understanding of the processes that may go wrong in earlier embryogenesis, of which there seems to be many. Studies on the presence of antigens on sperm may also turn out to be fruitful.

Spermatogenesis and the ovulatory cycle are ill-defined by comparison and it is in this area of research which we expect will benefit the most from the expanded program by which WHO hope to increase the understanding of the process of human reproduction. The aim of WHO's program is to develop safe and effective methods of regulating human fertility. Research is planned on a broad base. At present it is difficult to decide just what will have to be the best ways of improving physiological contraception. There is also the need to take into account the social mores which may mean that particular methods of contraception may not be acceptable in some countries.

The idea is to concentrate research on the basic processes which lead to sperm formation, maturation, and transport and also on the release fertilization implantation and early development of the egg. Even the stages of the ovulatory cycle are not at present known in much detail and just a slight increase in knowledge would cast a valuable light for example on what are the dangers of the rhythm method of contraception.

A large part of the research will concentrate on the biochemistry of steroid action on tissues of the female reproductive system. This certainly should offer the best prospects for improving contraception in the short term. Fears about the present contraceptive pill may be eased and better ones may be developed. The WHO program is also strong in that there will be set up centers which will conduct clinical tests for any possible fertility-regulating agents.

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WHO has decided that it is not sufficient to conduct research and then to let the results look after themselves. An integral part of the program is to help disseminate to other scientists the results which emerge from research on reproductive biology. Plans for WHO to establish a Documentation Center will no doubt be watched as an example of how communication can be improved in specific research areas.

This ambitious program of WHO will need more than the 500,000 dollars per year which it is spending at present on research in various aspects of human reproduction. These will continue but the new projects with a prospective income of 7 million for its first year is likely to have more impact. Funds for the program are being gathered from many sources.

It is of course no use providing answers if no one is willing to listen to them. However, since WHO will work internationally it's work will be likely to have an equally wide influence.—L.H.N.

Reference

1. Should Reproductive Biology be Encouraged? Nature, 233: 577, October 29, 1971.

Glucagon

The idea of balanced control of substances to maintain homeostasis is an old one. Calcium levels are regulated by parathormone which tends to raise blood levels of this ion and calcitonin which tends to lower it. Lymphocyte levels are regulated by thymosin which stimulates proliferation and thymostatin which causes lymphocyte lysis. Insulin lowers blood sugar and glucagon derived from the alpha cell of the pancreas tends to elevate blood sugar levels.

Administered glucagon increases blood glucose by accelerating glycogenolysis in the liver. Its structure is similar to secretin and this of course suggests a common origin. Glucagon, a polypeptide hormone increases the activity of phosphorylase kinase but does not affect muscle phosphorylase. Its mechanism of action is identical with that of epinephrine, i.e. stimulation of the formation of 3′5′ cyclic AMP by the adenyl cyclase system. This is a newly discovered pathway described by Sutherland and for which he received the Nobel Prize this year. However, glucagon in contrast to epinephrine stimulates glycogenolysis in low physiological concentrations and does not cause the elevation of blood pressure. Therefore, it has found clinical usefulness in circumstances of either acute or chronic hypoglycemia.

In pharmacologic doses glucagon exhibits cardiovascular actions and in the last three years attention has also been paid to the possible application of these effects clinically.[1] In an intravenous dose of 50 micrograms per kg., the hormone produces a slight increase in heart rate, a moderate increase in cardiac output but little or no change in arterial pressure or systemic vascular resistance. The effects from a single bolus last for approximately 15 minutes, but this can be prolonged by constant I.V. infusion.

These effects are regularly seen when glucagon is given to normal persons, patients with mild cardiac disease or patients with acute myocardial infarction who have experienced a first episode of congestive failure.[2] However, in patients with more chronic or prolonged heart failure, the hemodynamic effects of glucagon appear to be of lesser importance. The reason seems to be that in the failing heart, glucagon cannot activate adenyl cyclase activity and thus causes a lack of cyclic AMP release and therefore no demonstrably inotropic effect.[3]

By contrast, catecholamines such as isuprel retain their inotropic effect in the failing heart preparations. Thus if beta-adrenergic blockade is present, glucagon can still maintain cardiac action and this suggests another potential therapeutic use for this agent. For example, many patients are now receiving beta-adrenergic blocking agents such as propranolol for arrhythmias, angina pectoris, or subaortic stenosis. In such patients, severe episodes of acute heart failure may develop in association with arrhythmias or acute myocardial infarction and require emergency treatment. In this setting, the effects of catecholamines are blocked and glucagon may become a useful inotropic agent together with other conventional therapy.

Several studies have reported on the effects of glucagon on the A.V. conduction system and ventricular automaticity. Since glucagon increases A.V. conduction it might be useful in patients with incomplete A.V. block. Its apparent lack of arrhythmic properties by contrast with the catecholamines, suggests also that it might be useful in patients in whom arrhythmias develop with other agents such as catecholamines.

Antiarrhythmic properties of glucagon have also been described in digitalis toxicity.[4] However, this may be due to its chronotropic effect which would produce an overdrive suppression of ventricular arrhythmiac effects. Then, of course, there is the hyperglycemic effect associated with glucagon administration, leading to an insulin response which in turn produces a movement of glucose and K into cells. It is, however, not known whether this has any antiarrhythmic effect of any importance.

There are primary side effects of glucagon such as nausea and vomiting but these appear to be dose related and develop at dose levels above 50 micrograms per kg. Also prolonged administration may lead to hypoglycemia after the glycogen stores have been depleted. The reduction of serum K that follows glucagon administration is apparently of no clinical importance.[1] So far none of the polypeptide fragments of the glucagon molecule have been found to have as good a therapeutic response as glucagon itself.

The effects of glucagon are likely to be more important in a first episode of heart failure in a patient with little underlying cardiac disease. However, it is precisely in such patients that more standard measures of therapy are usually beneficial and of course should be considered as a primary attempt at control. Furthermore, in chronic heart failure, the hemodynamic effects of glucagon also appear to be of much lesser importance. Where then does glucagon find its place in therapy?

In the first place as noted above, it is useful in hypoglycemia. It may also be beneficial in selected cases involving beta-blockade toxicity, atrioventricular block, or acute heart failure or in patients sensitive to the production of arrhythmias by conventional inotropic agents. Thus, although glucagon does have cardiovascular effects with a useful therapeutic potential, except in hypoglycemia, it should probably be regarded only as an adjunct to the use of more standard therapeutic measures and not as the first line drug of choice.—L.H.N.

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1. Parmley, W. W.: The Role of Glucagon in Cardia Therapy, N. Eng. J. Med., 285: 801, September 30, 1971.
2. Diamond, G., et al.: Acute Myocardial Infarction in Man: Comparative Hemodynamic Effects of Norepinephrine and Glucagon. Am. J. Cardiol., 27: 612, 1971.
3. Epstein, S. E., et al.: Adenyl Cyclase and Myocardial Contractility. Ann. Intern. Med., 72: 516, 1970.
4. Cohn, K. E., Agmon J. Gamble OW: The Effect of Glucagon on Arrhythmias Due to Digitalis Toxicity. Am. J. Cardiol., 25: 683, 1970.

The U Waves In Cardiac Arrhythmias

(*Geriatrics*, 26: 140, 1971, Barnemann, S. D.) The U waves may merge with the T waves, become negative and may be easily confused with abnormal T waves. In general the height of U increases with greater duration of the preceding diastole and therefore greater filling of the heart. This may be due to increased stretch of the ventricular wall.

Abnormal U waves owing to cardiac arrhythmias are most pronounced in the chest leads V3-V5. They are partly responsible for the changes seen in the post extra systolic beats in atrial fibrillation and in atrioventricular block. They are often confused with primary T changes.

Medication with digitalis and phenothiazine and hypokalemia cause an increase in the height of U. Giant U are also observed in the syndrome of large Q-T intervals in the deaf mute.

In all these conditions the tendency to formation of extra systoles and even ventricular fibrillation is great.

Unknown is why giant U waves (usually confused with giant T waves) appear in patients with A-V block.—L.H.N.

Smoking And Neuroticism

(*Lancet* II, 770, October 2, 1971) Russel Meares, et al report on 102 smokers and 102 non-smokers with regard to their level of neuroticism, which was distinctly higher in the smokers. They proceed to give the reason.

Somatic manifestations of anxiety reflect activity of central excitatory or arousal mechanisms. By contrast, abnormally low levels of arousal are found in depressives.

Learning theory suggests that high arousal levels and "habit" formations are likely to be associated. This is perhaps why the smoking habit becomes more readily fixed in neurotic individuals.—L.H.N.

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SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, December 9, 1971

I. Attendance

Present in addition to the Chairman, Dr. K. F. Brandon, and the Vice-Chairman, Dr. D. A. Grendon, were: Drs. Weber, Jr., Cramer, Spitz, Backhus, Nolan, Granoff, Dean, Gardner, Hess, Bradley, Rem, Johnson, Ragland, Jr., Harwood, Pelz, Roch, Van Syckle, Friedberg, LaBella, Root, Jr. and Freedman.

Also present were: Mrs. Lindquist, Mr. Tomat, Dean Massey (UConn), Mr. Gordon, Mr. Olson, Dr. West (Clerk, NHCMA) and Dr. Richards.

Absent were: Drs. Fabro, Wilson, Palomba, Nemoitin, Luby, Harkins, vonGlahn, Dambeck and Klare.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of October 20, 1971.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Massimo Calabresi, 300 Ogden Street, New Haven (NH)—1/1/72

Michael E. Giobbe, 355 Prospect Street, Torrington (L)—1/1/72

Edna Hunkemeier, 520 West Avenue, Norwalk (F)—1/1/72

Joseph J. Mahoney, 120 Lafayette Street, Norwich (NL)—1/1/72

Wilbur J. Moore, 240 Maple Avenue, Cheshire (NH)—1/1/72

Charles V. Snurkowski, 487 Orange Street, New Haven (NH)—1/1/72

F. Erwin Tracy, 195 South Main Street, Middletown (M)—1/1/72

Date of Next Meeting

The Chairman set Wednesday, January 19, 1972, as the date for the next meeting of the Council.

III. Old, New and Special Business

Election of Student Members

It was VOTED to elect to Student Membership twenty-three Connecticut residents who are enrolled as students in American medical schools. A list of those elected will be published in an early issue of the Journal.

Report—Committee on 3rd Party Payments

It was VOTED to accept for filing a report of the Committee on the subject of physicians serving on utilization and review committees. Modifying a recommendation of the Committee, the Council further VOTED to approve the following statement: That it is the opinion of the Council of the Connecticut State Medical Society that a physician providing utilization and review services may accept reimbursement for such services. Finally, it was VOTED to refer to the Committee on PRO's Foundations and HMO's, for study and report to the Council, a "suggestion" of the Committee on Third Party Payments that consideration be given to the Society's arranging to provide utilization and review services on a paid basis to those requesting such services, with the Society, in turn, compensating the member physicians rendering the services.

CUPIS, Inc.

Request for Loan or Grant, CUPIS, Inc.: It was VOTED to receive for filing a letter from Dr. Bliss B. Clark, President, CUPIS, Inc., in which a request was made that the Council consider granting or loaning CUPIS the sum of $5,000 "to help enable CUPIS to reach its full (operating) potential". Having received the report of the Fiscal Committee on the subject request for funds, the Council further VOTED not to approve a loan or grant to CUPIS at this time.

Reports—Committee on Public Health

Proposed Study of "Etherington Committee Report" to the Governor: On recommendation of the Committee on Public Health, it was VOTED to appoint an Ad Hoc Committee to study those portions of the "Etherington Report" that have to do with health and medical care (health department, licensing, medical assistance, etc.), such Ad Hoc Committee to report its subject findings to the Council for possible use in legislative and related activities. It was further VOTED to request the Chairman of the Council to appoint the members of the Ad Hoc Committee, name the chairman thereof, and to include in the membership three members of the Committee on Public Health as follows: George N. Bowers, Hartford; Harold Lipton, Hartford; Susan S. Spencer, Torrington. Finally, it was VOTED to allocate the sum of $50 as a budget for the Ad Hoc Committee to cover such initial administrative costs as it may be necessary to incur.

CMS, Inc.

(a) *Mailing to the Membership*: It was VOTED to receive for filing notice given by the staff that a mailing to the membership had been completed on 12/2/71, such mailing having informed all members of the Society of the complete action taken by the House of Delegates on 11/17 concerning the recent decision of CMS, Inc. re participation in CMS contracts.

(b) *Report on Meeting with Insurance Commissioner*: President Weber reported verbally that, in accordance with the 11/17 directive of the House of Delegates, he had appointed a small committee of CSMS representatives (Dr. Weber, Dean, Grendon and Richards) and that such committee had met with the State Insurance Commissioner and staff on 12/7/71. Dr. Weber et al reported that while Commissioner Altermatt had expressed interest in and understanding of the views expressed in the resolution adopted by the House of Delegates, and would give further study to said views, it was his opinion as of now that his Department does not have jurisdiction over the matter of physician participation in CMS contracts. It was VOTED to receive this report for filing.

(c) *HCMA Legal Opinion*: The Council was apprised that the Hartford Association had obtained legal opinion from a Hartford law firm which concluded that "it is more likely than not that the Federal anti-trust laws apply to the activities of CMS (re participation in the Century Contract) and that CMS has, in fact, violated the anti-trust laws by attempting to monopolize prepaid medical care and/or by securing illegal tying agreements (with physicians) to restrict competition."

After prolonged discussion of this opinion, and based on a recommendation of the HCMA Board of Directors, the Council VOTED to adopt (13-7) a motion as follows:

That, acting for the Society, the Council retain the (Hartford) law firm of Howard, Kohn, Sprague and FitzGerald to proceed in court to obtain an injunction against the action of Connecticut Medical Service, Inc. to require participation (by physicians) in the CMS Century Contract as a condition of participation in the other CMS contracts.

In further pursuance of the action, it was VOTED that if and when an injunction against the CMS subject policy decision has been obtained, the Council call a special meeting of the House of Delegates to inform the House of the fact of the injunction and to seek approval from the House for a course of action (plan) to be followed subsequently.

Further Communication—Title XIX Medical Advisory Committee

It was VOTED to receive for filing a letter from the Director of Health Services, State Department of Welfare, which informed the Council that the new MAC proposed by Commissioner White would serve only in an advisory capacity to the Commissioner on Medicaid policy matters; that the new MAC would not serve in a claims review capacity (as did its predecessor) but that claims in question would be referred by the Department to "the Statewide Peer Review Committee" for evaluation and recommendation; and that Council approval of the appointment of the physicians selected by the Welfare Commissioner was again sought.

It was further VOTED to approve as being well qualified the physicians selected by the Commissioner for his appointment to the new Medical Advisory Committee he proposes to form, but to inform the Commissioner that the Council does not consider the new MAC to constitute the same "partnership" arrangement between the Society and the Department as did the two previous MAC's, a majority of whose members were nominated by the Council to serve in a peer review capacity (representing both geographical areas and the various types of medical practice).

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Finally, it was VOTED to inform the Welfare Commissioner that while the Society is proceeding with plans to form a "Statewide Peer Review Organization", it does not have such a PRO in being at this time; that, however, when the Society has a PRO in operation, he will be advised of its existence and invited to discuss its possible value to the Department in administering the Medicaid program; and to assure the Commissioner that the Council stands ready at all times to be consulted on matters of mutual interest or concern.

On the question of whether to retain the CSMS Liaison Committee with the Welfare Department in being, it was VOTED to continue the Committee in existence if only on a standby basis.

Reports—Committee on State Legislation

(a) *Proposals of the CSMS Section on Ophthalmology*: On recommendation of the Committee on State Legislation, it was VOTED to approve two proposals submitted by the Section on Ophthalmology as follows:

1. That Council of the Connecticut State Medical Society reaffirm approval of the hiring of ophthalmic assistants by ophthalmologists in Connecticut and reiterate the policy that such assistants' range of duties shall include any act or function assigned by the ophthalmologist for which the ophthalmologist deems his assistant qualified to perform, provided that the ophthalmologist remains fully responsible for the making of diagnoses and for the prescribing of therapy for his patients.
2. That the Council of the Connecticut State Medical Society authorize the CSMS Section on Ophthalmology to engage a legislative counsel at the expense of the members of the Section, such legislative counsel to operate in concert with the CSMS Committee on State Legislation and the CSMS legislative counsel in the area of the Society's legislative program that has to do with eye care.

(b) *Recommendation re Rhode Island Optometry Law*: The Section on Ophthalmology brought to the Council's attention the 1971 enactment of an amended definition of optometry by the Rhode Island legislature which allows optometrists to use drugs in the diagnosis and treatment of diseases of the eye and to made diagnosis of disease. Previously, optometrists were only allowed to determine and correct defects in visual acuity by mechanical means. Concluding that this definition further "opens the door" to the practice of ophthalmology by optometrists and that, if unchallenged, similar legislation would be promoted in Connecticut and other states, the Council VOTED to communicate by letter with the president of the Rhode Island Medical Society urging that the RIMS support the efforts of ophthalmologists to prevent the implementation of the new Rhode Island statute and, ultimately, to have the statute rescinded.

(c) *CSMS Statement re License Registration "Fee" of $150*: It was VOTED to approve and have transmitted to General Assembly's Finance Committee a statement on the new $150 (increased from $10) fee for registering physicians' licenses biennially. In brief, the statement contends that an increase of this magnitude converts the fee into a discriminatory "tax" on doctors; that it contributes to inflation of medical costs; and that the General Assembly should restore a cost-oriented fee for registration that can be justified on the basis of administrative expense to the state.

(d) *Legislative Commentary*: It was VOTED to receive for filing, and with commendation, a commentary prepared by Mrs. Ronald S. Beckett, Hartford, HCMA Legislative Committee chairman, in which a number of recommendations and suggestions were made as to how the Society's legislative program might be improved upon and made more effective. Copies will be sent to the members of the Committee on State Legislation.

Support of Resolution re "Open Staff" Policy

The Council was apprised of a resolution that had been adopted by the membership of the New Haven (City) Medical Association, and endorsed by the Board of Governors of the New Haven County Medical Association, which reaffirmed the important principle that hospital staff appointments should be granted to all physicians in a hospital's area of service who are ethically, morally and professionally qualified; urged the Board of Directors of the Yale-New Haven Hospital, Inc. to consider or reconsider the applications for staff appointments filed by three named physicians in the New Haven area in the light of this important principle; and urged the Board of Directors to delete from the present staff bylaws of the named institution provisions for limiting staff appointments on the basis of other than moral, ethical and professional qualifications.

Having considered the resolution, the adoption of the resolution by the NHMA membership, and the endorsement given by the Board of Governors of NHCMA, the Council VOTED to support the resolution and these actions and to communicate said support to the Board of Directors of the Yale-New Haven Hospital, Inc.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on December 9, 1971. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by an interested member of the Society.*

SUMMARY OF ACTIONS COUNCIL MEETING

Sunday, December 12, 1971

I. Attendance

Present in addition to the Chairman, Dr. K. F. Brandon, and the Vice-Chairman, Dr. D. A. Grendon, were: Drs. Cramer, Spitz, Backhus, Nolan, Granoff, Gardner, Hess, Johnson, Ragland, Jr., Harwood, Pelz, Roch, VanSyckle, Friedberg, Harkins, LaBella, Root, Jr. and Freedman.

Also present were: Mrs. Lindquist, Mr. Gordon (HCMA) and Dr. Richards.

Absent were: Drs. Weber, Dean, Fabro, Bradley, Rem, Wilson, Palomba, Nemoitin, Luby, vonGlahn, Dambeck and Klare.

II. Special Business

The meeting was called at the direction of the Chairman for the reason that several developments and questions had arisen concerning the Council's 12/9/71 action to initiate legal proceedings against CMS, Inc. which he felt should be brought to the attention of the Council before the 12/9 action was fully implemented.

The principal development was the announced intention of legal counsel to file for an injunction in a state court (instead of a federal court) and to base the reason for an injunction on claimed violation of a new Connecticut anti-trust law instead of the Sherman Anti-Trust Act (as proposed in the Council's 12/9 action).

It became evident that a majority of those present favored approval of the revised "plan" for taking legal action and, by a count of 14-4, it was VOTED to revise the wording of the subject 12/9 action to read as follows:

> That, acting for the Society, the Council retain the law firm of Howard, Kohn, Sprague and FitzGerald, Hartford, to proceed in court to obtain an injunction against the action of Connecticut Medical Service, Inc. to require participation (of physicians) in the CMS Century Contract as a condition of participation in other CMS contracts.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on December 12, 1971. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by an interested member of the Society.*

Placement Wanted

Anesthesiology—41 years of age; Interested in large hospital; respiratory therapy and chest disease. Available early 1972. Board Certified.

Emergency Room—28 years of age. National Boards. Wishes solo or group type practice in a medium size community in Connecticut. Would consider general practice along with a small group of other doctors. Available immediately. Contact: Robert W. Lisle, M.D., 4235 Falcon Courts North, McGuire AFB, New Jersey 08641.

General Practice—41 years old. Desires rural area. Solo practice. National Boards. W. Dean Pope, M.D., Box 490, Rangeley, Maine 04970.

General Practice—24 years of age. Wishes solo type practice in a small size community in Connecticut. Available early in 1972. Contact: Michael F. O'Connor, M.D., 15520 Windmill Pointe Drive, Grosse Pointe Park, Michigan 48230.

Institutional or Industrial Medicine: Solo, family practitioner in larger Connecticut community wishes to shift to institutional or industrial medicine. Board eligible. 63 years of age. Available early 1972.

Industrial Medicine—40 years of age; Connecticut and National Boards. Available early 1972.

Industrial Medicine—48 years of age; Connecticut license; Presently with firm in New Jersey. Wishes to relocate. Available immediately.

Internal Medicine—34 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut, in a medium size community. Connecticut license. Available immediately.

Internal Medicine—31 years of age, Certified, wishes group type practice in a medium size community in Connecticut. Available immediately.

Internal Medicine—Cardiology—34 years old; To relocate in Connecticut F.R.C.P. (C.). Eligible with National Boards. Desires hospital based or group practice position. Available immediately.

Internal Medicine—36 years of age; National Boards; Board eligible; Group or Associate practice; Available immediately.

Internal Medicine—62 years of age. Wishes solo or institutional type practice in Connecticut. Board Certified. Available December, 1971.

Internal Medicine-Cardiology—34 years of age, Eligible, wishes institutional type practice in a medium size community in Connecticut. Available immediately. Contact: Abnash C. Jain, M.D., 1926 W. Harrison, Apt. #1002, Chicago, Illinois 06012.

Neurology—41 years of age, wishes solo, group, or associate type practice in a medium or small community in Connecticut. Available immediately. Contact: George J. Vakkur, M.D., 2375 Terwood Drive, Huntingdon Valley, Pennsylvania 19006.

Neuropsychiatry—48 years old; Connecticut License in process. Solo, group, associate, institutional. Interested in E.E.G. Experience in research and teaching. Andre J. Angyan, M.D., Ph.D., 321 Orchard Drive, Pittsburgh, Pennsylvania, 15238 (412-828-5509).

Ophthalmology—30 years of age; National Boards, Board eligible; solo or associate type practice. Available March 1972.

Ophthalmology—31 years of age; Board eligible: National Boards; Solo or associate type practice.

Orthopedics—31 years of age, Eligible, wishes associate type practice in a large or medium size community in Southern Connecticut. Available immediately. Contact: Jeffrey S. Malka, M.D., 3225B Johnson Avenue, Riverdale, New York 10463.

Pathology—33 years of age. Connecticut license. Board Certified. National Boards. Presently in practice. Wishes group or associate type practice. Available immediately.

Pathology—46 years of age; Board certified; Prefers medium size community; Connecticut License; Available February 1972.

Pediatrics—29 years of age, Eligible with National Boards, wishes group or associate type practice in a large or medium size community in Connecticut. Available immediately. Contact: Jerald L. Zarin, M.D., 3D Collins Street, Westover AFB, Massachusetts 01022.

Radiology—42 years old; Board Certified; FLEX; Presently teaching. Available immediately.

Student or Occupational Health—59 years old N.Y.C. general surgeon wishes to relocate. Connecticut license. Available early 1972.

Surgery—48 years of age, presently in practice, wishes solo or associate type practice in a medium size community in Connecticut. Available immediately. Contact: James A. Cline, M.D., 2917 Tomahawk Drive, Rapid City, South Dakota 57701.

Surgery—35 years of age, wishes group or associate type practice in a large or medium size community in Connecticut. Available immediately. Contact: Pramod Shinghal, M.D., 115 Town Square Drive, Newport News, Virginia 23607.

General Surgery—37 years of age, Eligible, wishes solo or associate type practice in a medium size community in Connecticut. Available immediately. Contact: Robert J. Andrews, M.D., 2 Mechanic Street, Marblehead, Massachusetts 01945.

General Surgery—32 years of age; Board eligible; small or medium size community; solo, group or associate practice. Available immediately.

General Surgery—Late 50's; Board Certified; Presently in practice; Wishes to relocate in Connecticut. Over 25 years experience. Will consider emergency room or occupational health position. Available immediately.

General Surgery—41 years of age. Certified. Presently in practice. Wishes group or associate type practice in a medium or small size community in Connecticut. Available in January 1972. Please contact: Jose Peralta, M.D., 1916 Grand Concourse, Bronx, New York 10457.

General Surgery—32 years of age. Eligible with Connecticut license. Wishes group, associate or institutional type practice in Connecticut. Available immediately.

Placement Opportunities

Allergist: Wanted immediately to take over active practice and office; medium size (70,000) Connecticut community. New Haven area. Annual gross $58,000. Sole allergy practice in area. Call (203) 735-9501.

Physician for Emergency Room Duty—Splendid opportunity for qualified physician to work with medical group to provide around-the-clock coverage in Emergency Department for accredited General Hospital of 325 beds and modern supporting services. New England university town, two hour drive to New York and Boston. Hospital serves population of 125,000. Educational affiliation with university medical school. Liberal contract. Send curriculum vitae to Connecticut State Medical Society Placement Service, 160 St. Ronan Street, New Haven, Connecticut 06511.

Associate in General Practice: Busy general practice in Milford, Connecticut including pediatrics, Obstetrics and Gynecology, and some surgery (major and minor). New fully equipped office across the street from 200 bed open staff hospital. Boating, fishing and beaches 5 minutes from office. Yale-New Haven Medical Center and Yale cultural facilities 15 minutes away. Salary for one year with partnership to follow if agreeable. Please contact: Barry M. Winters, M.D., 73 Golden Hill Street, Milford, Connecticut 06460.

General Practitioner Preferred—Will involve travel to medicare facilities and review patient care standards. Travel to 30% nationally in one-two week spans. Salary to $30,000. Fee Paid. Contact: F-O-R-T-U-N-E Personnel, 60 Washington Street, Hartford, 547-0900.

Orthopedic Surgeon for Affiliation—in well established private practice in Connecticut. Arrangements open to discussion.

Director of Mental Health Training in a 1500 bed psychiatric hospital: dynamically oriented-unit system; progressive team approach; association with Yale University Departments of Psychiatry and Neurology. Directs the Psychiatric Residency training program, providing intensive training and experience with individual supervision in all psychiatric modalities; arranges visiting lectures and seminars. Opportunities to develop new programs for training and education in multidisciplinary areas. Board certification in psychiatry; eligibility for state licensure; administrative ability and teaching experience necessary. Salary commensurate with experience and training, liberal benefits, including free hospitalization. Please send resume and particulars to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut, 06457.

Director of College Health Service—Full time position; September, 1972; C. B. Crampton, M.D., Wesleyan University, Middletown, Connecticut 06457.

General Medicine and Internal Medicine—Northwestern Connecticut community seeking to attract practitioners. Associate type practice possible.

Occupational or Industrial Medicine—Two Connecticut post offices need staff physicians. Connecticut license. Part or full time.

Orthopedic Surgeon—Central Connecticut area. Community Hospital. Group practice with three other orthopedic surgeons.

Pediatrician—currently board-eligible or board certified. Full-time position. Salary negotiable. To practice family oriented medicine in a private, non-profit neighborhood health center. For further information please contact Evans H. Daniels, Jr., M.D., Medical Director, Community Health Services, Inc., 1023 Albany Avenue, Hartford, Connecticut, 06112. Telephone 549-1423.

Urology—Interested in an associate. Large, Southwestern Connecticut shore community.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Welcome, New Members

New London County

Louis Bender, M.D., 21 Norwich Avenue, Colchester, Conn. 06415.

Allen P. Borger, M.D., 29 Coult Lane, Old Lyme, Conn. 06371.

Henry Brown, M.D., 350 Montauk Avenue, New London, Conn. 06320.

Richard J. DiBella, M.D., 464 Ocean Avenue, New London, Conn. 06320.

Harold A. Engelke, M.D., Medical Arts Building, Gales Ferry, Conn. 06335.

John N. German, M.D., 350 Montauk Avenue, New London, Conn. 06320.

Joan A. Kadish, M.D., William Backus Hospital, Norwich, Conn. 06360.

Manuel E. Kadish, M.D., Brown School Road, RFD #3, Norwich, Conn. 06360.

Stephen E. Silver, M.D., 271 Montauk Avenue, New London, Conn. 06320.

Donald F. Sprafke, M.D., 41 Faire Harbour Place, New London 06320.

Tolland County

Howard Abbott, M.D., 57 Union Street, Rockville, Conn. 06066.

Neil H. Brooks, M.D., 1 Ellington Avenue, Rockville, Conn. 06066.

Gerald J. O'Brien, M.D., Johnson Memorial Hospital, Stafford Springs, Conn. 06076.

Litchfield County

U. Nagaraja, M.D., 62 Bank Street, New Milford, Conn. 06776.

Kenneth A. Nesbitt, M.D., Charlotte Hungerford Hospital, Torrington, Conn. 06790.

Alexander B. Snyder, M.D., U.S. Military Academy Hospital, Quarters 3053-A, West Point, New York 10996.

Richard Tiedemann, M.D., Hospital Hill, Sharon, Conn. 06069.

New Haven County

Sidney M. Baker, M.D., 150 Sargent Drive, New Haven, Conn. 06510.

Kenneth A. Bradford, M.D., 2 Church Street So., New Haven, 06519.

William T. Brown, M.D., 3 De Forest Street, Seymour, Conn. 06483.

James M. Burgin, M.D., 285 Broad Street, Meriden, Conn. 06450.

James T. Collins, Jr., M.D., 333 Cedar Street, New Haven, Conn. 06510.

Oliver T. Dann, M.D., 58 Trumbull Street, New Haven, Conn. 06510.

Leonard R. Farber, M.D., 111 Park Street, New Haven, Conn. 06511.

Norton S. Garber, M.D., 435 College Street, New Haven, Conn. 06520.

Mary Ann Gilliam, M.D., 111 Sherman Avenue, New Haven, Conn. 06511.

Isaac Goodrich, M.D., 2 Church Street, So., New Haven, Conn. 06519.

Bernard Z. Gore, M.D., 333 Cedar Street, New Haven, Conn. 06510.

Mortimer J. Hourihane, M.D., 385 Main Street, West Haven, Conn. 06516.

Richard J. Kostecki, M.D., 1211 W. Main Street, Waterbury, Conn. 06708.

Arthur H. Knowlton, M.D., 789 Howard Avenue, New Haven, Conn. 06504.

Ronald S. Kundargi, M.D., 1450 Chapel Street, New Haven, Conn. 06511.

Joseph M. Langner, M.D., 201 Main Street, Southington, Conn. 06489.

Jack P. Lawson, M.D., Griffin Hospital, Derby, Conn. 06418.

Sidney Lecker, M.D., 34 Park Street, New Haven, Conn. 06519.

Richard M. Linburg, M.D., 123 York Street, New Haven, Conn. 06511.

Elizabeth C. Lowry, M.D., 152 Broad Street, Guilford, Conn. 06437.

Richard E. Loyer, M.D., 1211 W. Main Street, Waterbury, Conn. 06708.

Massoud A. Marjani, M.D., 12 First Avenue, Waterbury, Conn. 06708.

Marie Mesaros, M.D., 789 Howard Avenue, New Haven, Conn. 06504.

Ira D. Mickenberg, M.D., V.A. Hospital, West Haven, Conn. 06516.

Daniel A. Myerson, M.D., Griffin Hospital, Derby, Conn. 06418.

Peter T. Naiman, M.D., 112 Broad Street, Milford, Conn. 06460.

Edwin C. Neville, M.D., 670 George Street, New Haven, Conn. 06511.

Maria Teresa P. Pardi, M.D., 666 George Street, New Haven, Conn. 06511.

George A. Robitaille, 56 Franklin Street, Waterbury, Conn. 06706.

Fernando P. Saracco, M.D., 2458 Whitney Avenue, Hamden, Conn. 06518.

Karen Shahnazarian, M.D., St. Mary's Hospital, Waterbury, Conn. 06702.

Hernan R. Silva, M.D., 1435 Chapel Street, New Haven, Conn. 06511.

George A. Silver, M.D., 60 College Street, New Haven, Conn. 06510.

Thomas J. Spicuzza, M.D., South Street, Middlebury, Conn. 06762.

Vincent F. Tremaglio, M.D., 561 Highland Avenue, Waterbury, Conn. 06708.

Byron H. Waksman, M.D., 310 Cedar Street, New Haven, Conn. 06510.

Leo V. Willett, Jr., M.D., 140 Green Road, Meriden, Conn. 06043.

Leonard H. Zamore, M.D., 186 Sherman Avenue, New Haven, Conn. 06511.

Joseph H. Zelson, M.D., 291 Lambert Road, Orange, Conn. 06477.

Howard V. Zonana, M.D., 123 York Street, New Haven, Conn. 06511.

Middlesex County

Joseph A. Bardenheier, M.D., Wildwood Medical Building, Essex, Conn. 06426.

Albert W. Bertuch, 195 South Main Street, Middletown, Conn. 06457.

Daniel J. Buchalter, M.D., 141 Broad Street, Middletown, Conn. 06457.

Donald E. Cook, M.D., 840 Boston Post Road, Old Saybrook, Conn. 06475.

Roger W. Cyrns, M.D., Rose Lane, Old Lyme, Conn. 06371.

Frank M. Geiser, M.D., Middlesex Memorial Hospital, Middletown, Conn. 06457.

John S. Goetcheus, M.D., Middlesex Turnpike, Essex, Conn. 06426.

Robert L. Reed, M.D., 5 InTown Terrace, Middletown, Conn. 06457.

Bernard F. Sheehan, M.D., 263 Main Street, Saybrook, Conn. 06475.

Robert Zavod, M.D., 25 InTown Terrace, Middletown, Conn. 06457.

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Doctor and Patient and the Law. R. Crawford Morris, LL.B. and Alan R. Moritz, A.M., Sc.D., M.D. Fifth Edition. The C. V. Mosby Company, St. Louis, 1971. 499 pp. $24.50.

Management of high-risk pregnancy and intensive care of the neonate. S. Gorham Babson, M.D. and Ralph C. Benson, M.D. Second Edition. The C. V. Mosby Company, St. Louis, 1971. 301 pp. with 62 illustrations. $16.50.

Speech Pathology. An applied behavioral science. William H. Perkins, Ph.D. The C. V. Mosby Company, St. Louis, 1971. 430 pp. $11.75.

Prevention Of Myocardial Infarction

(*Med. J. Aust.*, 1: 361, 1971, Laurie, W.) From the findings obtained by perfusion of over 2000 hearts from 3 racial groups it is confirmed that at least 75 percent of normal individuals are born with inter-arterial coronary anastomoses. The degree and character of such anastomoses vary widely from individual to individual.

The effects of exercise are important in lowering the incidence of coronary artery disease: exercise produces its beneficial effects by enlarging existing inter-arterial coronary anastomoses or by bringing into use the collateral vessels which involuted during childhood.

From experience in the study of the Zulus heart it is thought that jogging is one of the most practical and effective methods of exercise.—.H.N.

Characteristics Of Alzheimer's Presenile Dementia

(*Geriatrics*, 145, November, 1971.) Recent memory loss (2), time disorientation, 3 confusion. Average age of onset of this triad is 47.7 years and average age of the time of clinical diagnosis was 50.9 years.

The patient is aware of his own compromised intellectual function.

The lapsed social consequences of this disability is early amnesia, social impairment, occupational aproxia or proneness to accidents, increasingly impaired perceptual organization and perceptual disorganization.

Depressive and schizophrenic symptomatology also is not uncommon.

EEG changes occur early and characteristically include diffuse slowing with loss of the dominant alpha rhythm especially over frontoparietal areas.

The pneumoencephalogram may reveal generalized cortical atrophy or ventricular dilatation or both.—L.H.N.

SUMMARY OF PROCEEDINGS
HOUSE OF DELEGATES—SEMI-ANNUAL MEETING
Bridgeport, Connecticut—November 17, 1971

Reports

The House received reports of the Council and of the Officers, both of which are published in full at the conclusion of this summary. Accepted as information was a report on the activities of the Connecticut Medical Political Action Committee.

Principal Actions Taken

Continuing the procedure established several years ago, all business coming before the House was referred to, heard by and reported on by Reference Committees. Actions were taken on the reports of Reference Committees as follows:

(1) *Establishment of Financial Aid Fund for Medical Students:* As recommended by the Council, the House voted to (a) approve a subject report of the CSMS Committee on Cooperation with the Medical Schools of Connecticut, as amended by the Council; (b) approve the establishment of a CSMS Financial Aid Fund for students attending the Yale University and UConn Schools of Medicine, such funds to be implemented in 1972 on a one-year trial basis and be accomplished out of income received in 1972; and (c) approve the budgetary allocation of $6,000 in fiscal 1972, such allocation representing a funding grant of $3,000 each to the Yale University and UConn Schools of Medicine to be administered and used for the purposes stipulated in the report of the Committee on Cooperation with the Medical Schools of Connecticut. In brief, the fund will be used to make loans of not more than $500 in any one academic year to medical students who demonstrate need to the satisfaction of the university fund administrators. Loans will be repayable at any time up to seven years after graduation and, only after graduation, will carry a 3% per annum interest rate. A full report on the first year's experience will be made to the House of Delegates prior to the 1972 semi-annual meeting.

(2) *CSMS Loan to the Hartford County Health Care Plan (Foundation):* Amending a report and recommendation of the Council, the House voted to approve the following: That an interest-free loan of $5,000, drawn from the Society's reserve funds, be offered to the Hartford County Health Care Plan (Foundation) on a payback when feasible basis. If accepted by the Board of Directors of the HCHCP, the loan would be used to further the establishment of a health care foundation in Hartford County and to promote participation in the foundation among the members of the Hartford County Medical Association. In return, the Society expects to share the HCHCP experience in forming a foundation, such experience to be of potential value in the event that a statewide foundation is contemplated at a later date.

(3) *Resolution: Use of Amphetamines and Other Stimulants:* Being informed of allegations that over-prescribing of amphetamines and other stimulant drugs could contribute to illegal traffic in such drugs, the House voted to adopt, with minor amendment, a subject resolution introduced by the Council as follows:

RESOLVED: That the House of Delegates of CSMS urge all Connecticut physicians to continue to limit the prescribing and dispensing of amphetamines and other stimulant drugs to specific, well-recognized medical indications, and in moderate quantities, in order to aid in the control of drug abuse.

(4) *Resolution: CSMS Policy re "Physicians' Assistants":* In order to augment and clarify the Society's policy with respect to the use of qualified assistants by physicians, the House voted to include the following as an integral part of such policy:

RESOLVED: That the House of Delegates of the Connecticut State Medical Society affirm that it is the right and duty of the physician to do or cause to be done all things for the patient that the patient's medical care requires, and that the physician may properly delegate technical procedures to a properly qualified allied health worker; and be it further

RESOLVED: That the House of Delegates also affirm the principle that whatever privileges may at any time be granted either to allied health workers or to independent limited practitioners, such grant in no way circumscribes the physician's authority in the field and in no way restricts the practice of medicine by the licensed physician.

(5) *Resolution: Liaison Between Component Medical Associations and Local School Systems:* In keeping with a subject resolution adopted by the AMA House of Delegates in June, 1971, the House voted to adopt the following:

RESOLVED: That the House of Delegates of the Connecticut State Medical Society encourage the component County Medical Associations to establish liaison relationships with the school systems in their respective areas of jurisdiction and to provide appropriate assistance to such systems in the field of health education, particularly with respect to such critical subjects as drug abuse, smoking and health, venereal disease, alcoholism and quackery.

(6) *Resolution: Due Process in Review Proceedings:* Having been apprised that "due process" in review proceedings concerned with the professional conduct of physicians is receiving nationwide advocacy, the House voted to adopt a subject resolution as follows:

RESOLVED: That the House of Delegates of the Connecticut State Medical Society reaffirm its commitment to the principle that a physician whose professional conduct is reviewed by his peers shall be guaranteed a fair and objective hearing, including the guarantee of due process; and be it further

RESOLVED: That the House of Delegates urge the governing bodies and medical staffs of Connecticut hospitals to establish and utilize mechanisms for adjudicating internal disputes involving physicians which embody the procedure for due process outlined in the recently revised Standards of the Joint Commission on Accreditation of Hospitals.

(7) *Resolution: Endorsement of AMA "Medicredit" Bill:* On recommendation of the Council and the CSMS Committee on National Legislation, the House voted to adopt, with several amendments, a subject resolutions as follows:

RESOLVED: That the House of Delegates of the Connecticut State Medical Society endorse, in general, the basic concepts of the Medicredit Bill (S. 987; H.R. 4960) for national health insurance, sponsored by the American Medical Association, such general endorsement to place emphasis on the following principles which are considered by the House of Delegates to be essential to any and all proposals for national health insurance:

(1) Health insurance programs, private or public, should be pluralistic in form and in practice. Such programs should guarantee to each enrollee the right to obtain insurance protection and personal health services from professionally qualified providers of his choice among all those available in or to his area of residence.

(2) The standards of coverage for all insurance and prepayment programs approved for enrollment should be uniform, the coverage should be comprehensive, and the benefits and premium charges should be realistic for the enrollee's area of residence.

(3) The principle of "individual responsibility" should be implemented through the medium of reasonable co-insurance and deductible features.

(4) Recognition of ability to pay helps to minimize the need to use tax funds which more properly and economically could be directed toward providing adequate coverage for those less able to pay or unable to pay. The concept of progressive tax credits is one method by which this purpose could be achieved.

(5) A peer review mechanism for all services covered by insurance should be provided, such review to include charges, utilization and quality. In recognition of this need for review, the American Medical Association is sponsoring a PRO Bill (S. 1898; H.R. 8684) as a companion to its Medicredit Bill.

(6) There should be a statutory council composed of equitable representation of health service providers (including a significant number of private practitioners of medicine), health care insurers and the public ("consumers") which shall participate in formulating programs and policies for the administration of a national health insurance program. This council must approve all subsequent policy revisions and/or innovations and its decision shall

be binding on the federal agency administering the program. Similar councils should be established at local levels; and be it further

RESOLVED: That the House of Delegates direct that this endorsement and these principles be brought to the attention of the Board of Trustees of the American Medical Association and of all Connecticut representatives in the Congress and the members of the House Ways and Means Committee, and be pursued and promoted by the Society's Committee on National Legislation.

(8) *Resolution: Abandonment of Voluntarism by CMS, Inc.:* In his "Report of the Officers", President Frederick C. Weber, Jr., Greenwich, officially brought to the attention of the House the recent (10/26/71) memorandum received by all CMS Participating Physicians *not* participating in the Century Contract which informed them that unless they signed up for the Century Contract by January 1, 1972, the Board of Trustees of Connecticut Medical Service, Inc. would automatically terminate their participation in all antecedent contracts. In conjunction with his report, Dr. Weber introduced a subject resolution which, with several amendments, the House voted to adopt. In brief, the resolution "deplored" the decision of the CMS Board in this matter, pointed out several undesirable effects it might have on the voluntary system of health insurance and prepayment, and directed the President and a small committee appointed by him to seek an audience with the State Insurance Commissioner for the purpose of discussing with him in person the views and opinions on the CMS decision expressed by the Delegates in this resolution.

Since the full text of the resolution adopted has been sent by direct mail to all members of the Society, it is *not* reproduced herewith.

(9) *Resolution: Inequities Under the Medicaid Law Affecting Medicaid Beneficiaries and Practicing Physicians:* Introduced by the Council, in conjunction with the Councilors from the Windham Association, a subject resolution was amended and finally adopted by the House as follows:

Background Statement

In enacting the Medicaid Law in 1965, the Congress declared its intent that beneficiaries be entitled to obtain needed personal health services in their community areas of residence from providers of their choice and that the providers be paid for services on the basis of reasonable charges prevailing in those areas. The arbitrary freeze and cutback of Medicaid payments for physicians' services, imposed in 1969 by the U.S. Secretary of Health, Education and Welfare, have served to thwart these declared intentions of the Congress and have created unsatisfactory and inequitable conditions for both beneficiaries and physicians. These unsatisfactory and inequitable conditions have adversely affected Medicaid beneficiaries and practicing physicians throughout Connecticut and, particularly, in largely rural areas where a relatively small number of private practitioners are expected by the state to provide the bulk of needed medical services to Medicaid beneficiaries. In light of the foregoing, therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society again take cognizance of the unsatisfactory and inequitable conditions that are adversely affecting both Medicaid beneficiaries and practicing physicians throughout Connecticut, particularly in more rural areas, as a consequence of the arbitrary freeze and cutback on Medicaid payments for physicians' services imposed by the U.S. Secretary of Health, Education and Welfare in 1969; and be it further

RESOLVED: That the House of Delegates reaffirm its contention that the restrictions imposed by HEW in 1969 are serving to thwart the declared intent of the Congress that Medicaid beneficiaries have the right to choose their health service providers and that providers of services be paid on the basis of reasonable charges; and be it further

RESOLVED: That the House of Delegates again take cognizance of the fact that the Commissioners of Welfare and Finance and Control seem unwilling to pay private physicians their reasonable and customary charges, but do in many instances pay hospital clinics a higher fee for equivalent medical care; and be it further

RESOLVED: That the House of Delegates express the opinion that inequities in payments for physicians services could discourage physicians from settling in areas so affected; and be it further

RESOLVED: That the House of Delegates urge the Secretary of Health, Education and Welfare, in concert with the Commissioners of Welfare and of Finance and Control in Connecticut, to study these inequities in relation to the intent of Congress in enacting the Medicaid Law and to take such remedial steps as are needed to eliminate the inequities; and be it further

RESOLVED: That notice of this action be sent to the Governor of Connecticut, the Connecticut members of Congress, and the Secretary of Health, Education, and Welfare.

(10) *Resolution: Conjoint American Board of Nuclear Medicine:* Introduced by Mehdi S. Eslami, M.D., Waterbury, the House voted to adopt the subject resolution as follows:

WHEREAS: Full information concerning the *modus operandi* to be used by the Conjoint American Board (Boards of Radiology, Pathology and Internal Medicine) of Nuclear Medicine was not available to the AMA Council on Medical Education when the Council approved the founding of the Conjoint Board in June, 1971; and

WHEREAS: Board-certified specialists in Radiology, Pathology and Internal Medicine are expressing concern and dissatisfaction with the subsequently announced *modus operandi* of the Conjoint American Board of Nuclear Medicine, particularly with the announced policy of requiring reexamination and recertification of specialists already certified in nuclear medicine by their respective Boards; therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society instruct the Connecticut Delegates to the House of Delegates of the American Medical Association to support a resolution on the subject of "Conjoint American Board of Nuclear Medicine" at the forthcoming Clinical Session in New Orleans, such resolution to be introduced by the Delegate of the AMA Section on Radiology and to read as follows:

"RESOLVED: That the House of Delegates of the American Medical Association direct the AMA Council on Medical Education to request the Conjoint American Board of Nuclear Medicine to delay in proceeding further with its plan to conduct examinations and certifications for at least one year so that the AMA Council on Medical Education and the Liaison Committee on Medical Specialties can have an opportunity to discover whether the conditions under which the Council approved the Conjoint Board are being met, and also to gather more information and opinion by granting a hearing to concerned physicians and organizations."

(11) *1972 Budget:* As prepared and submitted by the Council, the budget for fiscal 1972 was adopted by the House, with membership dues remaining at $70.

(12) *Awards For Past CSMS Service:* Present to receive an engraved silver bowl in recognition of past service to the Society as Councilor-at-Large, 1970-71, was:

Stevens J. Martin, Hartford

Also eligible to receive awards for service, but not present, were:

Frank K. Abbot, formerly of Waterbury—Vice-Speaker, 1967-71

Reginald C. Edson, formerly of West Hartford—Secretary, 1969-71

Bernard A. Burnham, Waterbury—Treasurer, 1970-71

Oliver J. Purnell, Rockville—Councilor, Tolland County—1968-71

Honorary Degree:

An Honorary Degree in Medicine was bestowed upon John Franklin Enders, Ph.D., Sc.D., Boston, Massachusetts, "in recognition of his many outstanding contributions to the public health through his endeavors in the fields of bacteriology, immunology and virology."

(13) *Amendments to the Bylaws:* The House voted to adopt a series of amendments to the Bylaws which accomplished the following:

(a) Made the Committee on Allied Medical Services a standing committee of the House of Delegates.

(b) Changed the name of the Committee on Disaster Medical Care to the *Committee on Emergency Medical Services,* and redefined the duties of same.

(c) Changed the name of the Committee on Postgraduate Education to the *Committee on Continuing Medical Education.*

(d) Increased the allowed membership strength of the Committee on Rural Health from "not more than eight" to *"not less than eight"*.

REPORT OF THE COUNCIL

Kenneth F. Brandon, Hartford, Chairman

The Council has met seven times since the annual meeting of the House of Delegates last April. Detailed minutes of all Council meetings are received by the members of the House, hence this report will be limited to a summary of major matters considered by the Council and the actions taken thereon.

1. *Organization:*
   At the meeting of May 20, 1971, the Council honored me by electing me Chairman for 1971-72, and David A. Grendon, Sharon, by electing him Vice-Chairman for the same term.
2. *Interim Appointments, Etc.:*
   Included in the Handbook is a listing of the interim appointments made and resignations accepted by the Council with respect to officeholders elected by the House of Delegates at its April, 1971 meeting. Confirmation of these actions by the House of Delegates is requested. Of particular note is the appointment of Hilliard Spitz, New London, as Treasurer, replacing Bernard A. Burnham, Waterbury, resigned.
3. *Dates and Sites, Annual Meetings, 1972 and 1973:*
   Because of the space and accommodations required for annual meetings of the Society, and the necessity of reserving such accommodations well in advance, the Council has selected the dates and sites for the 1972 and 1973 annual meetings as follows: 1972—Hartford Hilton Hotel, Hartford, April 25-27; 1973—Hartford Hilton Hotel, Hartford, April 24-26.
4. *CSMS Policy re Use of "Combined (Obstetrical) Units":*
   Pursuant to the April, 1971 directives of the House of Delegates, the Council has taken actions as follows: (a) The Committee on Maternal Morbidity and Mortality was asked to reconsider its position on the subject policy. The Committee did so and reported to the Council that its position remained basically unchanged; i.e., that the use of available obstetrical beds should continue to be limited to "clean gyn cases" under the care of obstetrician-gynecologists. However, the Committee modified its position to include physicians who are not obs-gyn specialists but who have surgical privileges in gynecology. (b) The Council appointed an ad hoc committee of three members (Drs. Ragland, Bradley and Klare) to seek an audience with the Public Health Council for the purpose of advancing the position of the House of Delegates and seeking to have changes made in the Public Health Code which would make possible the implementation of that position. The Commissioner of Health elected to have the ad hoc committee heard by the Council on Hospitals, rather than by the Public Health Council, and on October 7, a hearing was held. It is understood that representatives of the Connecticut Society of American Board Obstetricians and Gynecologists also testified at the hearing. At this writing, it is our understanding that the Council on Hospitals will meet at a later date to weigh the testimony presented and arrive at a decision. The House of Delegates will be apprised of such decision when it has been made and announced.

   In addition to the foregoing, the Council has authorized the Committee on Hospitals to conduct a survey among hospital medical staffs concerning their attitudes toward the Society's subject position and a report on the survey is awaited. Also, the Council has advised several groups expressing dissent with the prevailing position that any member of the Society has the right to submit to the House of Delegates for consideration a resolution calling for a change to be made. At this writing, no such resolutions have been received.
5. *CRMP:*
   By comparison with the recent past, the Council has spent relatively little time since last April on matters having to do with activities of the Connecticut Regional Medical Program. In part, this is due to the fact that responses from CRMP to a number of questions raised previously by the Council and the House of Delegates are still being awaited, and, in part, because it has been impossible for the Council or the Society's representatives on the CRMP Advisory Board to keep abreast of the myriad new activities that are being initiated month by month. Under joint study by the Society's Committee on Statewide Medical Planning and representatives of CRMP is the possibility of conducting a comprehensive analytical survey of the private practitioner and the private practitioner's office as a primary point of patient entry into the health care system and as a mechanism for providing medical service of high quality at reasonable cost. CUPISS has dropped one of its S's and left the jurisdiction

of CRMP to become a private agency called CUPIS, Inc. Our president, Dr. Frederick C. Weber, has accepted membership on the CUPIS Board of Directors and will keep us informed as to developments. Despite this transfer of management, the Council will continue to seek assurance that the principles of "confidentiality" and "informed consent" are utilized effectively to protect the proper interests of patients.

6. *Peer Review Organizations, Foundation and Health Maintenance Organizations:*

   At the meeting of June 17, 1971, on recommendation of our Ad Hoc Committee on Peer Review Organization Planning, the Ad Hoc Committee was discharged and, in its place, a new Committee on PRO's, Foundations and HMO's was appointed, with Sidney L. Cramer, Hartford, as chairman. The Committee is charged with undertaking "an in-depth study of these related subjects and to make recommendations to the Council and House of Delegates concerning the possible roles to be played by the Society in the several areas, and to serve in an educational capacity for the enlightenment of the membership (on said related subjects)". While the Committee is not yet prepared to submit a definitive report or recommendations to us at this time, assurance is given that it has been moving actively to fulfill its assignments and will be able to give us the benefit of its studies in the near future. It is our understanding that first priority has been given to the ways and means of setting up a statewide PRO, with county and/or regional components, in order to be prepared to meet the requirements of whatever subject legislation may be enacted by the Congress. Foundations and HMO's are by no means being ignored by the Committee but it is felt that, due to the complexity and enormous expense associated with forming either foundations or HMO's, a "go slow" approach is the prudent one for all concerned.

7. *CSMS Financial Aid Fund for Medical Students:*

   Having received successive reports from our Committee on Cooperation with the Medical Schools of Connecticut that a substantial number of students attending the Yale University and UConn institutions are having difficulty making ends meet in the matter of financing their education, the Council voted to accept the final report of the Committee and its recommendation that the Society establish financial aid funds at each of the schools so that needy students could borrow up to $500 in any given academic year. The report of the Committee, as amended by the Council, is presented for approval by the House of Delegates.

8. *Medical Advisory Committee, Connecticut Blue Cross:*

   Having been apprised that Connecticut Blue Cross is forming an MAC of twelve practicing physicians to advise the CBC administration on matters of policy, utilization review, etc., the Council made a request that "up to six" of the physician members of the MAC be designees of the Society. The reply ultimately received from the CBC Executive Committee stated that the Society's request could not be granted because of previously established policy.

9. *CSMS Endorsement of the AMA "Medicredit Bill":*

   Having been apprised that an increasing number of state and county components of the American Medical Association have taken official actions to endorse the AMA's "Medicredit Bill" for national health insurance, the Council requested the Committee on National Legislation to make a careful study of said bill (S. 987; H.R. 4960) and to make a report and recommendations to the Council concerning the Society's endorsement of same. On October 20, 1971, the Council voted to adopt a subject resolution, submitted by the Committee as its report. A resolution on CSMS endorsement of "Medicredit" is recommended by the Council for adoption by the House of Delegates.

10. *Resolutions in Keeping with Recent AMA Actions:*

    At the August meeting, having received the report of our Delegates to the AMA on the Atlantic City meeting (6/20-24/71), the Council voted to submit to the House of Delegates a series of four resolutions which are in keeping with subject actions taken by the AMA House of Delegates as follows:

    Subject: Use of Amphetamines and Other Stimulants

    Subject: CSMS Policy re "Physicians' Assistants"

    Subject: Liaison Between Component Medical Associations and Local School Systems

Subject: Due Process in Review Proceedings

11. *Publication and Distribution of 1971 CSMS Relative Value Guide:*

Pursuant to the actions taken by the House of Delegates on April 27, 1971 to approve the report of the Committee on Third Party Payments and a "rough draft" of a proposed 1971 CSMS Relative Value Scale, the Council, in Cooperation with the chairman of the Committee on Third Party Payments, has moved as rapidly as possible to get the RV copy in final form for submission to the printer. In keeping with opinions expressed at the April meeting of the House, and on recommendation of the Committee chairman, the Council voted to change the title of the document from "Relative Value *Scale*" to "Relative Value *Guide*". Based on present time projections, it is anticipated that the Guide's publication and distribution to the membership will be accomplished early in 1972.

12. *Activities of the Public Affairs Committee:*

Pursuant to the April 27 directive of the House of Delegates, the Committee on Public Affairs has stepped up its political education activities, including promotion of COMPAC membership, in cooperation with the COMPAC Board of Directors. Having approved an outline of program development for 1971-72, drafted by the CSMS staff, the Committee undertook its first major function on September 30 in the form of a "Leadership Conference". Attended by more than 100 medical leaders at state, county and local level, a morning seminar on Peer Review Organizations, Foundations and Health Maintenance Organizations was presented in cooperation with the new CSMS Committee of the same name. The afternoon session was conducted in the form of a workshop on public affairs, with both Society spokesmen and outside panelists featured. It is always difficult to evaluate the success or failure of projects of this kind, but as far as could be determined from on-the-scene comments from participants, our Committee on Public Affairs has every right to feel that the daylong program was rated excellent and to be encouraged to arrange additional functions of this type.

13. *Proposed CSMS Loan to the Hartford County Health Care Plan (Foundation):*

Early in 1970, having accepted a report of the Committee on Third Party Payments on the subject of "Foundations", the Council noted that the Hartford County Medical Association had already made some initial inquiries into the feasibility of establishing a Hartford County Health Care Foundation and voted to urge the HCMA Board of Directors "to undertake a pilot HCMA membership survey on the foundation approach . . . and report on the results of such survey to the Council". At the Council meeting of October 20, 1971, the HCMA Councilor, Carl W. Johnson, Thompsonville, reported that the Hartford Association had incorporated a Health Care Plan (Foundation) in July of this year and that the new corporation was engaged in organizing the Plan administratively and in taking initial steps to enroll HCMA members as Foundation participants. Noting that the financial obligations associated with these activities were proving to be substantial, and hypothesizing that a successful Foundation operating in Hartford County would prove ultimately to be of value to physicians throughout the state, Dr. Johnson transmitted to the Council a request of the HCMA Board of Directors that the Society make a "grant of $5,000 (minimum)" to the Health Care Plan to help defray the costs of these organizational activities. After a considerable period of discussion, and in light of being informed that no funds for such a grant out of income would be available in either 1971 or 1972, the Council voted to offer the Hartford Health Care Plan a loan in the amount of $5,000 out of the Society's reserves and to recommend to the House of Delegates that such a loan be authorized by the House in accordance with the recommendations of the Council.

14. *The Budget for 1972:*

As prepared by our Fiscal Committee, the Council has approved a budget for 1972 and recommends its approval by the House of Delegates. Published in the Handbook is the proposed budget in detailed form. Our Treasurer, Dr. Spitz, is prepared to present a summary of the significant changes made from the 1971 budget in the matter of allocations, etc. and it is suggested that he be asked to make this presentation by the chairman of the Reference Committee to which the item is assigned for hearing. For emphasis, it is again noted here that the allocation of $6,000 to the proposed CSMS Financial Aid Fund for Medical Students is clearly identifiable in the budget and that the House is asked to give specific approval to the inclusion of such allocation in conjunction with its action on the financial aid program itself. Also, for information only, the House of Delegates is advised that the Council has rescinded the "Dutch Treat Libation Policy", which was implemented as of January 1 of this year, and has again authorized reasonable charges for libations to be made to the Society. The principal reason for this rescinding action was that the policy proved to be impractical to administer, despite cooperation by all concerned. In connection with this change in policy, the Council has urged all committees and other groups to utilize the Society's headquarters building for meetings to the fullest extent possible and to consider substituting buffet-type food at the building for the more time-consuming sit-down dinners. The buffet format has been used extensively by some of our most active committees and they report that their time is conserved and their productivity increased as a consequence.

15. *Proposed Amendments to the Bylaws:*

    While not an integral part of the Report of the Council, attention is drawn to four proposed amendments to the Bylaws which have lain on the table since the annual meeting of the House of Delegates in April. These appear in the order of business for this meeting and are published in this Handbook. It is assumed that they will be heard by a Reference Committee and acted on by the House in accordance with established procedure.

16. *Awards:*

    Attention is also called to the listing of awards to be made which is included in the order of business for this meeting. The bulk of these will be presented to members who have made contributions of service to the Society as officers or as Councilors from component County Associations. Since Frank K. Abbot, Waterbury, was leaving Connecticut for California in early July, the Council arranged to present to him an award for service as Vice-Speaker of the House of Delegates at its meeting on May 20, 1971. The conferring of an Honorary Degree in Medicine upon John F. Enders, Ph.D., Brookline, Mass., was approved by the House of Delegates on April 27, 1971. The awarding of the Honorary Degree will take place at the luncheon served during the mid-day recess of the House and the award ceremony will be concluded with remarks in response by Dr. Enders.

17. *Resolution on Effects of Inequitable Medicaid Payments:*

    Earlier this year, a resolution was presented to the Council on behalf of the Windham County Medical Association which protested "discrimination" practiced by the Department of Welfare which resulted in inequitably low payments being made to physicians practicing in Area IV (Windham County) for services rendered to Medicaid beneficiaries. The resolution was referred (in accordance with the resolves) to the Committee on Third Party Payments for study and report. At its meeting on October 20, 1971, the Council accepted the subject report of the Committee for information but concluded that the "discrimination" alluded to in the WCMA resolution was actually statewide in application and had resulted from the freeze and cutback (to the 75th percentile) on Medicaid payments imposed in 1969 by the Secretary of Health, Education and Welfare. However, the Council recognizes that in largely rural areas of the state, such as Windham County, there are no public clinics to which Medicaid patients can be referred and it therefore falls to the practitioners in those areas to provide needed medical services to all patients for whom the state assumes responsibility. For these reasons, the Council voted to direct the staff, in consultation with the WCMA Councilor, to draft for presentation to the House of Delegates at this meeting a resolution which would embody the sense of the Council's deliberations on the matter just described. Such a resolution has been drafted and the Council recommends its adoption by the House of Delegates.

18. *Resolutions Transmitted to AMA House of Delegates:*

    At the meeting on October 20, the Council voted to adopt and transmit to the New Orleans meeting of the AMA House of Delegates, 11/28-12/1/71, three resolutions which are described as follows:

    (1) *The Private Practice of Medicine:* The thrust of the resolution is to reaffirm that individual private practice has demonstrated its ability to provide quality care at reasonable cost, and to urge that it be

retained as an integral part of the American health system.

(2) *Rising Hospital Costs:* The resolution again draws attention to the activities of tax funded agencies to promote full-time, salaried chiefs of services in hospitals, and asks for a study to be made of the effects of such activities on charges made to patients.

(3) *Financing of Education as a Hospital Function:* The resolution is directed to the broad question of including the costs of education as a function of hospitals in the charges made to patients for hospital care, and urges that a study be made to determine how such costs could be borne equitably by the public-at-large.

The foregoing report is for information only.

19. *Conclusion:*

In concluding this report, the Chairman of the Council extends sincere thanks to our President, Dr. Frederick C. Weber, Jr., of Greenwich, for the excellence of his leadership; to the members of the Council for their dedication to duty and their maintenance of good humor during many hours of often heated debate; and to the Executive Director, the Associate Director and the entire staff for the competent services they continue to render month after month. To chair the Council is indeed a privilege and an opportunity for service that is deeply appreciated by this reporter.

REPORT OF THE OFFICERS

Frederick C. Weber, Jr., Greenwich, President

At this semi-annual meeting of the House of Delegates, I am honored to present to you a report on behalf of the officers of the Society.

As the House Ways and Means Committee conducts its hearings on the myriad proposals for National Health Insurance, it is interesting to note the differing points of view held by various organizations engaged in financing, providing, and teaching patient care.

The Administration is leaning, hopefully, toward the Health Maintenance Organization (H.M.O.) concept as a major mechanism for providing health services for large groups. H.M.O.'s are largely experimental at the moment and may ultimately be able to prove their alleged merits with respect to quality and cost, but it is a recognized fact that the initial funds required to establish an operating H.M.O. are substantial. The A.M.A. has offered its Medicredit Bill, the principles of which you will be asked to consider for endorsement during this meeting.

The ongoing debate as to how health care should be financed has finally brought to light the realization that a major portion of the entire Federal budget would have to be expended on providing the benefits called for by some of these plans. Those who are responsible for raising the needed funds through taxation have been forced to reconsider whether this nation, even with its vast resources, can actually commit so large a percentage of its budget to the area of health care and still carry on its many other essential programs.

This realization appears to have led to a slowing down of the rush toward taxfunded national health insurance and to a greater appreciation of the pluralistic approach to solving health care problems.

The medical schools have been drawn back into the important area of patient care and are beginning to reorient their curricula to teaching students to be patient care providers, with a consequent de-emphasis on specialization and research.

The Student American Medical Association has initiated a program to promote general training and practice in areas of the country less well supplied with doctors. SAMA is implementing this program, called "MECO", under which a medical student will spend a period of a month or so during vacation periods with a practicing community physician to learn the problems he faces first hand. The Society has been asked by SAMA to cooperate in the implementation of the program in our state, and the request has been referred to our Committee on Cooperation with the Medical Schools of Connecticut for study and report to the Council as to what contribution the Society and its members can make to this worthy project.

These evolving changes in perspective and direction encourage me to believe that we still have opportunity to make intelligent input into the governmental processes that are sure to play a major role in determining how health services will be provided and financed in the future. I recognize that common sense and carefully thought out plans are apt to come up against serious opposition from the counter forces of political expedience, pressure from organized labor and other groups, but I do not think that we are quite yet on the road to the complete nationalization of medicine in the pattern of England and Quebec. I was not so optimistic in this regard one or two administrations ago.

There is an increasing interest among patients in donating their organs after death for transplants. The Eye Bank has an efficient procedure for making corneas available. The Kidney Foundation could accumulate many more organs for use if it would set up an efficient method for acquiring kidneys at the time the donor dies. This problem should be submitted to the Committee on Organ and Tissue Transfers for joint study with the Kidney Foundation in order to work out a suitable plan for accepting donor organs at a time when the public is showing a favorable attitude.

I assume that, by this time, all or most of you have become aware of the recent decision of the Board of Trustees of Connecticut Medical Service, Inc. regarding participation in the Corporation's Century Contract. From a number of membership sources, the Society has received comments highly critical of this decision and been urged to make an official statement concerning it. After consultation with several of my fellow officers, with our executive staff and with our legal counsel, I have decided to bring this matter to the attention of this House of Delegates officially for careful consideration and appropriate action. I have elected to do this by introducing a resolution, and by recommending that the House so consider and so act upon it. It is my expectation that the Speaker will refer the resolution to a Reference Committee for hearing and it is my hope that all of you will take part in the discussion that ensues.

It is indeed a privilege and an honor to serve this Society as one of its officers. The office of the President carries with it greater responsibilities

President of the Society, Frederick G. Weber, Jr., (left) congratulates John F. Enders, Ph.D., after conferring upon him an Honorary Degree in Medicine at the Semi-Annual Meeting of the House of Delegates in Bridgeport on November 17, 1971.

than any one person could expect to discharge in full, and I am deeply appreciative of the generous support given me by my fellow officers, the County Association councilors and our staff. I take this opportunity, also, to express thanks to the officers and members of the County Associations for the uniformly cordial hospitality extended to me as a guest at their semi-annual meetings.

ENDERS AWARDED HONORARY DEGREE IN MEDICINE

The following remarks were delivered by the President of the Society when he awarded John F. Enders, Ph.D., an Honorary Degree in Medicine.

I feel personally privileged to be president of the Connecticut State Medical Society on one of the infrequent occasions on which, by unanimous vote of the House of Delegates, we are to bestow an Honorary Degree in Medicine on a most worthy recipient. I say infrequent because, during the period of the past forty years, the Society has made only four such awards even though the authority to do so is as old as our Charter—granted in 1792.

From 1792 until 1814—the year in which what is now the Yale University School of Medicine graduated its first class of student physicians—the Medical Society passed on the qualifications of all who aspired to practice medicine in Connecticut and conferred the degree of Doctor of Medicine on those deemed to be qualified. Subsequent to 1814, the Society voluntarily transferred the principal exercise of its authority to Yale University and, since that time, has limited its awarding of degrees in medicine to those of an honorary nature.

Our Bylaws provide that we may honor, as a degree recipient, a "person, not a physician, distinguished in the sciences of medicine or for contribution to human welfare." The man we honor today certainly qualifies on both counts. Through his research in the fields of bacteriology, immunology and virology, he has probably had an influence on the health—and perhaps even on the lives—of more people throughout the world than all of the physicians assembled in this room put together. Practitioners everywhere have been able to provide better medical care to their patients as a consequence of his outstanding work.

The investigations he made of the poliomyelitis virus, jointly with two co-workers, led to the development of the Salk-type vaccine for immunization against that dread disease, and for this achievement he and his co-workers received the Nobel Prize in Medicine and Physiology. Later, he made important contributions to the development of a vaccine against measles.

Since 1947, he has held the post of Chief of Research in the Division of Infectious Diseases at the Children's Hospital Medical Center in Boston. He has taught at the Harvard University School of Medicine, as Professor of Bacteriology and Immunology, and is currently University Professor Emeritus. He has presented papers before many of the world's most noted scientific and medical organizations, and his articles have appeared frequently in the scientific journals of many lands and have been translated into many languages.

The world-renowned scientist of whom I am speaking in John Franklin Enders— a man who truly belongs to Connecticut. Although his home is now in Brookline, Massachusetts, he is a native of West Hartford and a summer resident of Waterford. Recently, he and members of his family donated a large tract of land to our state to be used for conservation purposes.

Dr. Enders Expresses Thanks

November 23, 1971

Dear Dr. Weber:

The proceedings last week at the luncheon of the Delegates of the Connecticut State Medical Society keep coming to mind. I was deeply moved by the kindness and warmth of all those present. Nothing of this sort that has happened to me has given me more pleasure.

I especially appreciated your remarks and wish to thank you for them once again.

It was a most pleasant surprise to find my friends Bob McCollum and George Miller at the meeting. Their presence made me feel very much "at home". I also enjoyed seeing Dr. Foote again as well as my Yale classmate Dr. Wakeman and having the opportunity to meet and talk with Dr. Hess.

The history of the granting of the honorary degree in medicine is extraordinarily interesting to me as a native of Connecticut and a graduate of Yale College.

All in all it was an occasion which I shall always remember with great satisfaction and I shall always be grateful to you and the other people who were responsible for it.

With all good wishes.

Sincerely,
John Enders

As one peruses the list of degrees that Dr. Enders has received—and merited well, one cannot help but find it impressive. However, we will be forever grateful to the late Dr. John R. Paul, of New Haven, for bringing to our attention the fact that a degree in medicine is still missing from the list. It is, therefore, especially appropriate that the Connecticut State Medical Society should now bestow a degree in medicine on one of Connecticut's most distinguished sons.

With this introduction, I now ask Dr. Enders to rise and join me at the podium.

Sir, under the authority granted to the Connecticut State Medical Society by its Charter, enacted in 1792 by the Connecticut General Assembly, it is my privilege as the president of the Society to bestow upon you—John Franklin Enders—this Honorary Degree in Medicine in recognition of your many outstanding contributions to the public health through your endeavors in the fields of bacteriology, immunology and virology.

Congratulations! Members of the House of Delegates and distinguished guests, I present to you John Franklin Enders, M.D.

Meeting Notices

The information on this "notices" page is offered as a service of all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the month preceding, date of issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

GENERAL

April 25-27, 1972—Tuesday-Thursday
180th Annual Meeting of the Connecticut State Medical Society
Theme: Clinical Pharmacology
Hartford Hilton, Hartford

September, 1971-May, 1972
Lecture Series—Each Tuesday
Basic Sciences As Related to Clinical Medicine: Infectious Diseases, Coronary Care Problems, Diagnosis and Treatment of Tumors
Lawrence and Memorial Hospitals
New London, Connecticut
Contact: Edward Gipstein, M.D.

February 23-25—Wednesday-Friday
Diagnosis and Management of Infectious Diseases
University of California, Center of Health and Science, Los Angeles

March 20-24—Monday-Friday
Specifically Treatable Diseases
University of Pennsylvania School of Medicine, Philadelphia

GASTROENTEROLOGY

February 7-9—Monday-Wednesday
Digestion and Disorders of Digestion
Mayo Graduate School, Rochester, Minnesota

INTERNAL MEDICINE

January 26—Wednesday
CSMS Section on Internal Medicine; Connecticut Society of Internal Medicine; American College of Physicians
Hunt Memorial
Scarborough Street, Hartford
Contact: Benjamin V. White, M.D., Hartford

SURGERY

January 27—Thursday
Annual Meeting of the Connecticut Chapter of American College of Surgeons
Park Plaza, New Haven
Contact: Francis M. Hall, M.D., Hartford

February 2-5, 1972—Friday-Saturday
Symposium on Problems of the Female Breast as Related to Neoplasms and Reconstruction
Memorial Sloan-Kettering Cancer Center, New York City

WOMEN'S AUXILIARY

February 8—Tuesday 10:30 a.m.-2:30 p.m.
School Day For Doctors' Wives
Discussion of terminology used in new health care plans. Several speakers representing various health care plans in Connecticut.

Special Article

Medical Progress A Century Ago: A New Medical Curriculum In America

Hebbel E. Hoff, M.D., Ph.D.*

The basic discoveries of earlier decades came to be exploited at an accelerating pace in the latter decades of the 19th century. The new chemistry of Lavoisier was one of the most powerful forces in this development. Especially so in medicine was his demonstration that, in their sum, the processes involved in respiration represented no more than the slow combustion in the body of carbon and hydrogen in an atmosphere of oxygen to produce carbon dioxide and water. With them, he showed an amount of heat was released equal to that produced by the in vitro combination of the same amount of oxygen with an equivalent amount of charcoal and hydrogen. This demonstration of the fundamental identity of processes in the living world and the inorganic world led in 1828 to the synthesis of Urea by Wöhler and to the beginnings of biochemistry.

The slow perfection of the microscope made it possible around 1840 for Schleiden and Schwann independently to enunciate the cell theory establishing the fundamental building block of all animal and plant organisms, and demonstrating the basic interrelationship, through the common denominator of the cell, of all living creatures. Out of this grew on the one hand the doctrine of evolution and on the other the special subjects of histology, pathology, microbiology, embryology, and somewhat later the neurone doctrine. Modern medicine as we know it was indeed established during these busy decades as the new scientific background of the structure and functions of man in health and disease was worked out and carried from the laboratory into the hospital, and the impetus of these years is still strong and continuing.

So it was with the new science of electricity. It had an extensive early history, and the extraordinary power of the "electrical fluid" was fully recognized, especially toward the end of the 18th century when the leyden jar and elaborate static electric machines made it possible to accumulate and store considerable charges. But it was only in the last decade of the 18th century that Luigi Galvani discovered that a couple made of two dissimilar metals could stimulate nerves and muscles. Galvani believed that such a couple discharged an indwelling animal electricity which in turn caused the muscle to contract. Volta for his part confirming Galvani's experiment was able to demonstrate that the two metals were the *source* of the electricity that stimulated the nerve or muscle, via potentials generated mainly at the two metal-fluid interfaces. Volta's most convincing proof came when he arranged dissimilar metals "in series" or "in battery", to use an artillery expression, to produce a relatively long lasting source of what he now began to call "the electric current." Of course these studies quickly stimulated Oersted's discovery of electromagnetism and Farraday's work on electrical induction and the electric motor and generator were just beginning to take a reliable form in 1871. In the meantime Galvani turned out to have been right about the existence of animal electricity, and after Bernstein had measured the time course of a nerve impulse in 1868 the way was open to the development of electrocardiography, electroencephalography and the exploitation of neurophysiology. It is not by chance that Erlanger and Gaser in their Nobel prizewinning work used a variant of Bernstein's rotating "rheotome" as the mechanical sweep generator for their cathode-ray tracings, or that Adrian in his equally important and equally rewarded work on sensory discharge used as a recording system the capillary electrometer that Lippmann had learned about from Kühne soon after Kühne came to Heidelberg as Professor of Physiology in 1871.

The world of 1871 was, as it is now, facing the

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spectacle of war, that between the growing Empire of Germany and the somewhat tired Empire of Napoleon the Third in France. Its effects are equally a part of our present-day political troubles, for the Germans having besieged and forced the capitulation of Paris and the whole of France, the Paris commune inherited the defeat, and a civil war followed more terrible than the war that brought it on; Karl Marx watched the first inept uprising from London, and assessed its lessons for the future; there would be no "half-measures" and "unnecessary magnanimity." When the Soviet cosmonauts flew in the Voskhod they brought with them as a sacred relic a ribbon off a communard flag.

In America the country was making its comeback after the civil war, and just a hundred years ago the revolution in medical education was in the making that has brought us to the present moment. In 1869 Charles William Eliot had been elected president of Harvard University at the age of 35, by no means unanimously and not without hesitation. He had graduated from Harvard College in 1853, second in his class, with a broad foundation in mathematics, while, because of close relations with few outstanding professors, he had had the almost unique experience, for an undergraduate of those days, of participating in the work of the chemical laboratory and in mineralogical field trips. Staying on in the College as tutor in mathematics and chemistry he resigned his appointment at Harvard because he failed to be promoted after five years as an assistant professor. His eyesight preventing him from joining the army—the civil war was then in progress—he left for Europe where he studied the sciences, but principally investigated the new developments in university organization that were then in full course of development, particularly in the burgeoning German universities. Returning to Boston in 1865, he taught for four years at the Massachusetts Institute of Technology before being appointed, somewhat reluctantly it would appear, President of Harvard University in 1869.

Here Eliot began by reforms in the College—the elective system bears his imprint—and in the University, drawing together the separate facilities that until then only loosely bore their Harvard affiliation into a firm organic and academic relationship. The Medical School was one of the first to feel the weight of his insistence on the establishment of academic control and university standards in its programs and practices, and especially in its teaching. In his first annual report of 1871, he wrote forthrightly that "the whole system of medical education in this country needs thorough reform" and at a meeting of the medical faculty reported by Oliver Wendell Holmes, where some of the new rules were laid down to an unhappy faculty, one of them asked plaintively why after being left alone for eighty years the faculty was suddenly asked to change everything. Eliot replied "There is a new President."

Just what the change Eliot envisaged amounted to was set forth in David Cheever's Introductory Lecture before the entering medical class at Harvard on October 2, 1871. In part he told the new students:

> "On this eighy-eighth anniversary of the opening of our Medical College, it is my peculiar privilege to welcome you to the old School, with its mode of instruction reformed, amplified, systematized, made progressive.
>
> Here in America nothing is allowed to grow old. Change, and that change often progress, attacks every art, every calling, every institution. As the human body is itself subjected to a constant interchange of atoms, and dies at last through incessant use, so the art of medicine changes season by season, is modified by fashion, by progress of the sister sciences. The medical "knowledge and the medical practices of to-day are not those of twenty years ago; neither should the medical education of to-day be that of former years.
>
> With no abatement of deference and of gratitude for all that the Medical Department of Harvard University has taught us in the past, it is not assumption to hope that its progress in the future will be still more marked. *For in this ancient and stable University there has come to pass a change in medical education, more radical, more thorough, and, as we believe, more beneficial in its effects on the future of our profession, than any other since the foundation of our college.* (Italics H.E.H.).

Then, briefly describing the virtual chaos of the older curriculum which offered the whole curriculum in a 4-month course repeated identically year after year without sequence (attendance at two such courses was adequate for the MD degree), Cheever briefly presented the essence of the new curriculum.

> "The changes in the mode of instruction to which all new students who enter for our medical degree will be subjected, and in which we cordially invite all students who have partially completed their studies, here or else-

> where, to join, are chiefly these:—Instruction will be uniform and continuous throughout the entire year; and progressive throughout three years.
>
> Studies and students will be classified, and divided into a three years course.
>
> "Examinations will be distributed throughout the three years. The mode of teaching will be more demonstrative, practical and experimental, and less didactic, than formerly.
>
> Lectures, recitations and practical exercises will, as heretofore, all be used as modes of instruction. But the proportion of recitations to lectures will be larger than before; while demonstrative and experimental study, in the Dissecting Room, the Chemical Laboratory, the Microscope Room, the Physiological Laboratory, and the Autopsy Rooms; and clinical study in the Hospitals and Dispensaries, will be very greatly increased, and supplant, to a certain degree, the college lecture rooms.
>
> To assure this advantage of the demonstration, the experiment, the clinical study and the recitation over the lecture, it is essential that all the class take active part in those exercises. *And this they will be expected to do, since every student will have his place and time in the anatomical, physiological and chemical laboratories, and in the microscope room; and laboratory work will be as much required of him as attendance at lectures.* (Italics H.E.H.).
>
> We would, however, by no means do away with the old lecture system. The lecture brings the teacher face to face with the whole class; gives a living significance to the dry teaching of medical treatises; enables the lecturer to select only those parts of written medicine which are valuable; and to add and enforce "much practical wisdom that is not found in books. We intend, therefore, to offer you full courses of lectures on all those subjects which cannot be made wholly demonstrative, or experimental; and some of which, as the anatomical, surgical and pathological departments, possess a wealth of illustration in plates, preparations and cabinet specimens."

Speaking of the premedical preparation Cheever emphasized that these too, must be academically sound and based on the university:

> "Whatever studies, then, cultivate the perception and the judgement constitute the best preliminary education for the medical profession. The natural sciences, chemistry, physics, natural history, mathematics, educate these faculties more than languages, literature or history; for the latter are better adapted to fluent speech, good memory and elegant tastes. The classics, however, are not to be thrown aside; since a fair knowledge of Latin and Greek is of inestimable value to the reader of medical literature; but such modern languages as the French and German, teeming with scientific research and medical publications, are, beyond doubt, the most directly useful to the physician.
>
> Scientific schools, and schools of technology supply the kind of preliminary knowledge the medical student needs.
>
> "The academic department of our own University has been so far modified, of late, as to very well meet these requirements. But such is not the case in the undergraduate curriculum of most other colleges.
>
> The natural sciences, the dead languages to a certain degree, and the modern languages are, then, to be especially cultivated by the youth who means to study medicine."

Of the preclinical sciences as we know them, Cheever recognized Chemistry, Anatomy, Physiology, and Materia Medica, and all were to be taught in the first instance by observation and experiment. Anatomy, Chemistry, and Physiology were to be taught in the first year, and he had this to say about Physiology:

> "Physiology, comparatively a modern science, has made great advances of late years, and is still in a transition state. As influencing and correcting the *practice* of medicine it is the most important of either the departments. Without the truths which it has taught us of the functions of different organs in health, in disease and under the influence of various medicinal agents, the science and practice of medicine would sink back a century.
>
> The physiological effect of various lesions and the physiological action of drugs, are the modes of studying this department most directly conducive to practical results. Experiments have also often been verified by the absence or modification "of certain functions in disease. We may all of us conduct a series of harmless experiments on ourselves in health. By Dr. Hammond in this country, and by numerous experimenters abroad, very useful results have been arrived at in this way. *Physiology is learned, like Chemistry, only by experiment.*

> *It is to be pursued in a laboratory, and chiefly by experiments on the lower animal* (Italics H.E.H.). The study by vivisection of the humbler members of the animal kingdom appears a very cruel one. And so it may, thoughtlessly, be made. We deprecate unnecessary repetitions of experiments; carelessness in causing pain, or consecutive mutilations of the same animal. But for the necessity and propriety of physiological vivisections, poisonings and medications of the lower animals, we would put in an earnest plea. By this path alone can therapeutics advance in certain knowledge. Experiments on the vital functions, and on the action of drugs are of the last importance to the wellbeing of man."

Finally Cheever pointed to the Internships as a necessary part of the educational program:

> "To recapitulate the order in which we would advise you to study medicine—Chemistry, Anatomy, Physiology.
>
> Pathology, Surgery, Materia Medica, Medical Chemistry. Science and Practice of Medicine, Therapeutics, Obstetrics.
>
> "Medical Jurisprudence, Specialties.
>
> We have thus provided a *three year's course.* Would that it could be made a four year's one. At present, however, this is as long as many of you can devote to professional study. For the more fortunate few who have a fourth year at their disposal, there are two ways in which it can be profitably spent; either in a hospital here, or by studying in Europe. If you can live a year in a hospital as house-physician or surgeon, you will gain more practical knowledge than you can possibly do in an equal time abroad, because you will here treat cases, and therefore remember them. Where but one can be had, we should prefer the year in hospital at home to Europe. Where both can be enjoyed, a year or two abroad is extremely valuable. It enables you to pursue one or more special branches farther than you can in this country. You medical education, so far from being finished, is only begun when you get your degree."

Thus, just a century ago, the full pattern of (1) a general scientific and cultural premedical experience, (2) a sequential series of preclinical and clinical sciences, (3) the emphasis on learning by observation and experiment as well as from lectures, (4) the importance of the clinical clerkship, (5) the need for an internship and (6) the need for the whole program to be located in a University setting with full academic control was firmly planted in this country, even though it would take nearly forty years and a Flexner report before the idea was fully established.

(This is the first of a two-part series)

NOTICE TO CONTRIBUTORS

Members of The Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Detailed instructions to contributors appear in the last section of *Connecticut Medicine.* Adherence to the instructions will prevent delays both in acceptance and in publication.

Please send them to:

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Electrocardiogram of the Month: Effects of a Psychotropic Drug on the Electrocardiogram Imipramine

Manchester Memorial Hospital
Manchester, Connecticut

Prepared by
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An increasing number of cardiovascular effects of phenothiazine derivatives and tricyclic antidepressants[1,2] are being recognized. A direct effect upon myocardial function resulting in a diminution of cardiac output as well as impairment of cardiovascular reflex mechanisms have been reported.[3] Hypotension, cardiomegaly, congestive heart failure, cardiac arrest, arrhythmias, conduction disturbances, and other electrocardiographic changes may occur.

Electrocardiographic abnormalities described in imipramine toxicity and overdosage include supraventricular and ventricular arrhythmias, prolongation of QT interval, abnormalities of the ST segments and T waves, and conduction abnormalities such as partial or complete antrioventricular block, widened QRS complexes and bundle branch block. Electrocardiographic changes are reported in patients on therapeutic as well as after ingestion of excessive amounts of the drug.

The following electrocardiograms were taken two hours and four hours respectively after ingestion of excessive amounts of imipramine (Tofranil) by a 44 year old woman. There was no past history of heart disease, and an electrocardiogram taken five years previously was normal. These tracings represent the type of arrhythmia, conduction disturbance and ST segment changes that may be found in imipramine toxicity.

The first electrocardiogram (Figure 1) reveals P waves occurring at regular intervals of 76/minute, isoelectric in leads 1, 3, AVR and AVL, and inverted in leads 2 and AVF. The PR interval in lead 2 measures 0.08-0.10 seconds. Each P wave is followed by a widened QRS complex measuring 0.16 seconds (lead 2) and having a left bundle branch block configuration. This is interpreted as a junctional rhythm with left bundle branch block pattern. The blood potassium level was normal 4.0 mEq/l.

The second electrocardiogram (Figure 2) demonstrates normal sinus rhythm of 90/minute, normal P waves, PR interval of 0.17 seconds, and normal QRS complexes 0.08-0.09 seconds in duration. Nonspecific depression of ST segments is present in several leads. Forty-eight hours later, these abnormalities had also returned to normal.

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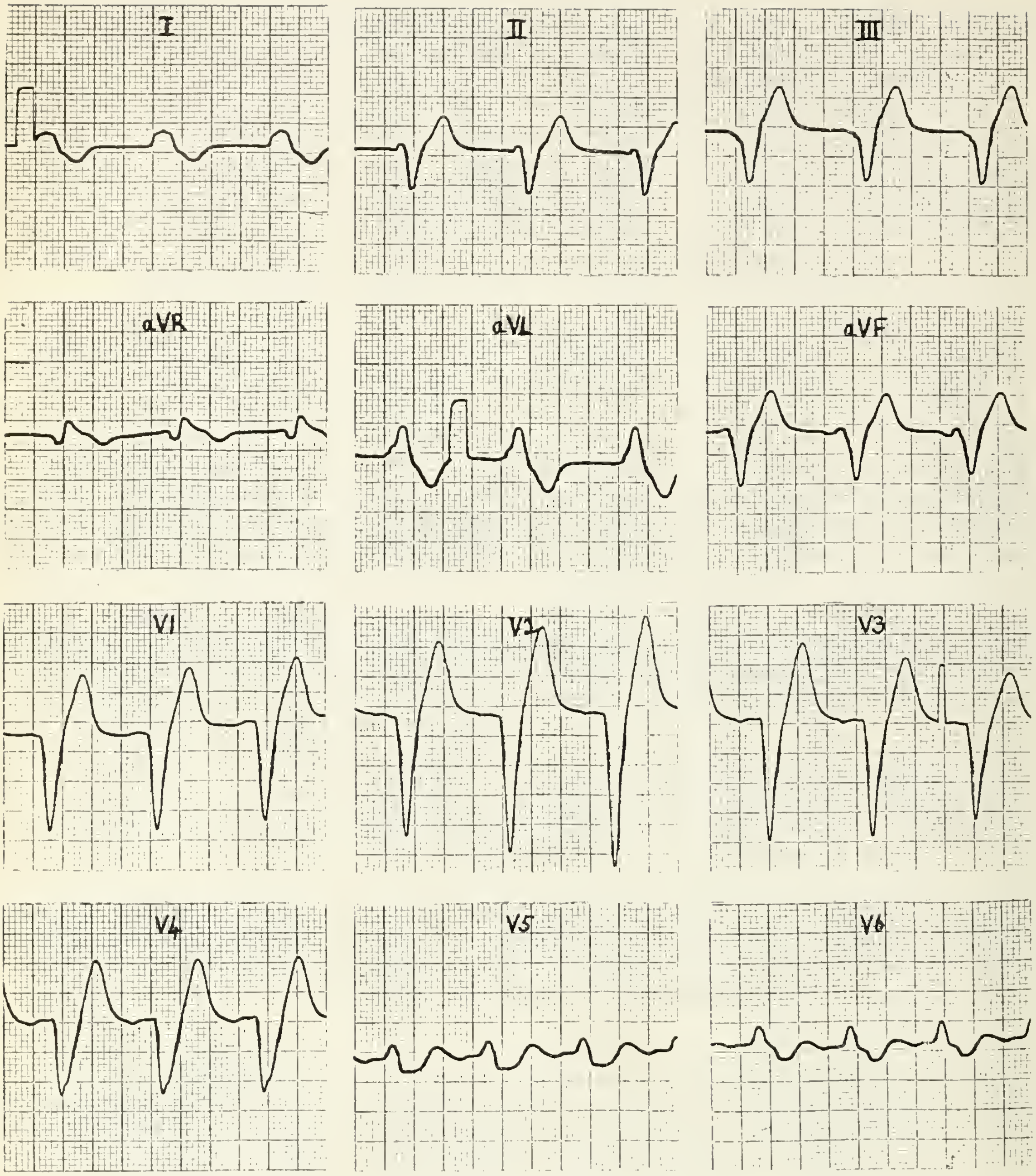

Figure 1

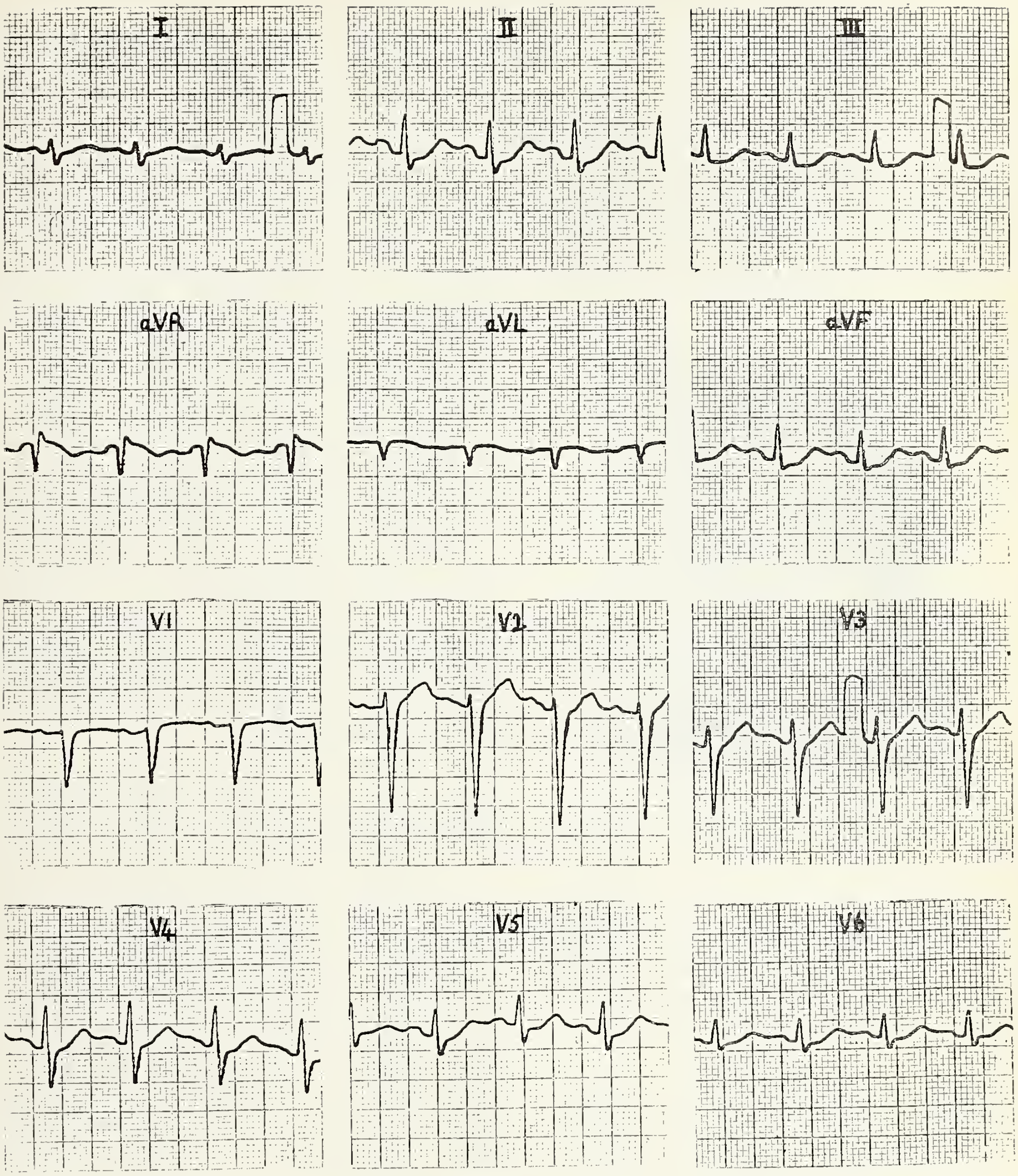

Figure 2

OBITUARIES

Victor L. Szanton, M.D.

1905-1971

Dr. Victor L. Szanton, a member of the Editorial Committee of *Connecticut Medicine*, died in the Yale-New Haven Hospital on November 7, 1971. He was 66 years old. He was the guest editor of the Pediatric Issue and the Allergy Issue of *Connecticut Medicine*. He was a practicing pediatric allergist.

He was born in New York City in 1905. He received his B.A. from the University of Alabama in 1932 and his M.D. from Duke University in 1936. From 1936 to 1937 he had a rotating internship at Watts Hospital in Durham, North Carolina; a pediatric internship at Jewish Hospital, Brooklyn, New York, 1937 to 1938 and a residency in pediatrics at Mt. Sinai Hospital, New York, 1938 to 1939.

Because of his conviction that a competent specialist should have a background of general practice, Dr. Szanton took on a solo general rural practice in the Maine woods in Jackman, Maine. He was the only physician within a radius of 75 miles in all directions. There, he was also Town Health Officer, Selective Service examining physician, an overseer of the poor, U.S. Public Health Officer and sometime physician to German war prisoners in the prison work camps. Lacking local hospital facilities he carried out practice as realistically as possible. He often made house calls by horse and sled, snowshoes, railroad hand car, freight train caboose, airplane, motorboat and pack horse which took him into the deep woods lumber camps.

He established model well baby clinics, immunization programs, a course in nutrition, prenatal care, a school lunch program, a youth center and the first use of Maine's first mobile dental unit. Even though he carried on a demanding isolated general practice, he attended pediatric meetings in Boston as well as lectures and rounds at Children's Hospital in Portland, 180 miles away and other hospitals. He felt that this gave him a sense of giving specialist-quality care despite the demands of a rural, solo general practice.

It took until 1947 to find some one to take over his practice. It was then that he migrated to Derby, Connecticut where he established a pediatric practice. He pioneered specialization in the lower Naugatuck Valley. He re-established his relationship with Mt. Sinai Hospital in New York at which hospital he was appointed at that time as assistant clinical attending physician. Additional appointments secured were to the staff of Yale-New Haven Hospital, the Hospital of St. Raphael in New Haven, Griffin Hospital in Derby and St. Vincent's Hospital in Bridgeport.

At the Hospital of St. Raphael he developed a quality clinic for allergic children. This clinic continues to function there. In 1960, at the Hospital of St. Raphael, Dr. Szanton organized a Symposium on the Allergic Child in New Haven. This served as a model for subsequent regional symposia throughout this country and Canada.

In 1957, Dr. Szanton published a report of a salmonella epidemic starting in the newborn nursery at Griffin Hospital, a four year study. Another outstanding contribution to the literature was Allergic Paracusis, a previously unrecognized syndrome. He lectured internationally on his discovery of this syndrome.

He was Associate Clinical Professor of Pediatrics and Allergy at the Albert Einstein School of Medicine, New York, New York; Attending Pediatric Allergy, Griffin Hospital, Derby, Connecticut; Attending Pediatric Allergy, Hospital of St. Raphael, New Haven; Attending Pediatrics, Yale-New Haven; Past Director, Pediatric Allergy (out-patient clinic) Hospital of St. Raphael, Assistant Clinical Pediatrician, Pediatric Allergy, OPD, Mt. Sinai Hospital, New York.

He was a consultant at the White House Conference (1960) Committee for the State of Connecticut; Regional Consultant Jewish National Home for Asthmatic Children, Denver, Colorado; Ad Hoc Committee Legislation for the Battered Child-State of Connecticut; Immediate Past Chairman: Pediatric Section, American College of Allergists, Board of Regents, American College of Allergists.

He was a Diplomate of the National Board of American Medical Examiners, Diplomate National Board of Pediatrics, Diplomate American Board of Pediatrics (Pediatric Allergy).

He was a member of numerous medical societies which included the American Medical Association, Connecticut State Medical Society, New England Allergy Society, American Academy for Advancement of Science, New York Academy of Science, New England Pediatric Society, Hezekiah Beardsley Medical Society, Connecticut Allergy Society, American Academy of Allergy (Fellow), American College of Allergists (Fellow), American Society of Certified Allergists, International Society of Allergology, American College of Chest Physicians, American Association of Medical Writers.

He took a profound interest in education, not only among his medical peers but also among the general public. He took interns into his office to acquaint them with office practice of medicine. He lectured to the Fire Departments, Police Departments, and telephone crews on bee stings as well as on other topics.

As Medical Library Committee Chairman at the Griffin Hospital in Derby, Connecticut, he succeeded in organizing a previously chaotic library into a well stacked and well catalogued facility.

Dr. Szanton was a tremendous humanist. He combined both the science and the art of medicine in his practice of medicine. He gave of himself unstintingly to his patients who considered him their friend as well as their physcian. He was a contributor to his profession as a teacher, author, editor, and researcher.

Surviving are his widow, Willette; two sons, Jonathan and Jeremy; a sister, Mrs. Beatrice Tobey, and a grandchild.

Oscar Rogol, M.D.

James R. Miller, M.D.
1886-1971

Dr. James Raglan Miller was born in Hartford on February 7, 1886. He graduated from Yale College with a B.A. degree in 1907, and received his M.D. from Johns Hopkins in 1911—A.O.A.

There followed some two and a half years training in Frauenkliniks and Pathology in Freiburg, Munich and Vienna, which at that time included service under Aschoff and Wertheim.

In 1914 he returned to Baltimore for Obstetric residency training at the Hospital for the Women of Maryland, and also served as Clinical Instructor in Obstetrics at Johns Hopkins where J. Whitridge Williams was chief.

Dr. Miller began private practice in Hartford in 1915 with appointment that year to Hartford Hospital as Assistant Obstetrician and Gynecologist.

Soon after the United States entered World War I he was in Europe again with the Army Medical Corps 1917-1919, both in France and later Germany.

Return to active practice was marked by involvement in many hospital and civic activities including the institution of the Prenatal Clinic in 1923, and with several others, organization of the Tumor Clinic which later spread to the State General Hospitals and was developed into the justly famous Tumor Registry in the Connecticut State Department of Health.

In 1930 he was certified by the American Board of Obstetrics and Gynecology as a charter member and in 1942 and 1946 was chairman of the Department of Obstetrics & Gynecology in Hartford Hospital. During all these years he had a number of scientific papers published.

Besides an enviable reputation as a skilled operator, he liked to teach, stimulating House officers and younger attendings toward the goal of better patient health and care.

And for Dr. Miller this goal extended beyond local hospitals to City Clinics, to county and State medicine and even internationally into World Health.

He left practice in 1950 after 35 years of active service and died in the Hartford Hospital at the age of 85 on October 26, 1971.

To give some idea of the range of his professional interests and accomplishments, a somewhat shortened list of activities is appended: Physician in Chief Hartford Dispensary for many years; Director of the American Cancer Society 1946-50; Chairman Hartford County Chapter Nat'l Foundation Infantile Paralysis 1941-45; President of the Council Social Agencies Hartford 1924-26; U.S. Delegate World Health Organization 1948-49; Member of the Committee on Chronic Illness 1950-57; Fellow American College of Surgeons (Bd. of Govs); member of Hartford Medical Society; President of the Hartford County Medical Association 1938; President of the Connecticut State Medical Society 1947; American Medical Associate (Trustee 1950-55) Delegate from Conn 1941-45; New England Surgical Society (President 1944-46); American Gynecological Society (Treasurer 1947-49) and New York Obstetrical Society.

He demanded a high quality of performance in himself, "and hated the approximate."

Derick A. January, M.D.

Lucien A. Geraci, M.D.
1891-1971

Lucien A. Geraci, M.D. of 1199 Whitney Avenue, New Haven, Connecticut, physician and surgeon in the area for 42 years died November 2, 1971 in the Hospital of St. Raphael, New Haven, Connecticut, after a short illness at the age of 80.

Dr. Geraci was born in Palermo, Sicily February 1, 1891, the son of the late Frank and Jennie Pata Geraci. He came to this country as a child with his parents and after preliminary preparation in the New Haven Schools he graduated from Yale University Class of 1913. He received his medical education at the College of Physicians of Surgeons, Columbia University, N.Y. and his M.D. Degree from that institution in 1917. After internship at St. Vincent's Hospital, in New York City he was commissioned a first lieutenant in the U.S. Army Medical Corps, during World War I.

In 1919 he returned to New Haven, Connecticut where he became a member of the staff of Grace-New Haven Hospital and practiced there as a physician and surgeon from 1919 to 1952. During this time he was a member of the State, County and Local Medical Societies and became certified as a Fellow of the International College of Surgeons.

In 1952 Dr. Geraci left active private practice of medicine and surgery and was appointed senior physician at the Veteran's Home and Hospital, Rocky Hill, Connecticut. He held that position and served it with distinction until ill health forced his retirement in 1961. Since then he devoted his time to his family. Besides his wife Mrs. Lucy Geraci he leaves one daughter Mrs. Robert B. (Janet) Broadbent, of Hamden, one son Lucien A. Geraci Jr., of New York City, one brother Alfred Geraci of Dobbs Ferry, N.Y. and two grandchildren.

John J. Mendillo, M.D.

Disturbances Of Cardiac Rhythm During Anesthesia And Surgery

(*JAMA*, 216: 1615, 1971, Bertrand, C. A. et al) The authors monitored 100 patients undergoing surgery during general anesthesia. Supra ventricular and ventricular arrhythmaias developed in 84 patients particularly at the time of intubation and extubation. The cardiac patients had a higher incidence of ventricular arrhythmias.

Special attention is urged to the two periods with highest arrhythmic potential.—L.H.N.

Beta-Receptor Blockade And Myocardial Effects Of Cardiac Glyosides

(*Circulation Research*, 28: 109, 1971, Koch-Weser J.) This author found that propanolol reduced the contractility by 85 percent of kitten papillary muscles. However, it did not modify the action of digitalis. They conclude that release of myocardial norepinephrine plays no role in the action of cardiac glycosides on the heart.

The implication is that patients receiving propanolol for angina do not lose their ability to respond to cardiac glysosides if they had contractile support that is lost through propanolol.—L.H.N.

Prevention Of Athersclerosis With Calcium

(*Medical Counterpoint*, 3: 34, November 1971.) Residents of areas in which water has a high calcium content have less cardiovascular disease than the rest of the population. Recent studies have shown that the ingestion of calcium in amounts above the daily nutritional requirements diminish experimental atherosclerosis.

H. Yacowitz, et al used rabbits. Their serum cholesterol levels are usually around 25 mg. per 100 ml. They were fed a high-fat, high-cholesterol ration that raised the level to an average of 1400 mg. per 100 ml. The animals developed severe athersclerosis when given a normal or low calcium intake. When given 10 times the amount required to maintain calcium nutrition, the amount of athersclerosis was distinctly less.

This ration at first caused a lowering of the blood lipid concentrate but after a few months on the diet this change disappeared.—L.H.N.

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OUR PRESIDENT'S MESSAGE

Oliver Wendell Holmes once said: “The great thing in this world is not so much where we stand at it is in what direction we are moving. To reach the port of Heaven, we must sail with the wind and sometimes against it—but we must sail, and not drift or lie at anchor.”

This is particularly true in the year of 1971-72 for in 1972 the Woman's Auxiliary to the American Medical Association will reach its 50th birthday. What other group can look back through fifty years of devoted service on the distaff side? Tremendous changes have taken place in these fifty years.

From the friendly, comforting office of the family physician, we have moved to the complex, hurried atmosphere of medicine today filled with printed forms in triplicate, insurance forms, government returns and repeated welfare demands.

As the American people have moved from a state of individual enterprise motivated by the desire to be self-supporting, proud and free, the medical profession has been forced into a position where it is often difficult to retain the close physician-to-patient relationship so important to good medical practice. As a result we have witnessed a growing animosity on the part of the general public to the image of the physician.

Everything is changing—our technology, our society—you and me, too. When you dare to risk—dare to innovate, dare to seek, dare to differ, dare to understand, dare to act—you involve yourself in influencing and shaping this change in direct ways.”

We have a responsibility as members of the medical family. The word “advertising” has many meanings, but for the Auxiliary, only one, and that is to tell others what we are doing. “Doing business without advertising is like winking at a girl in the dark. You know what you are doing but nobody else does.”

When you “advertise” you first decide whether you want to build a publicity program or a public relations program. The two are entirely different. Publicity is easy to create, but public relations is letting people know *who* you are, *what* you believe and *what* you stand for. Someone defined public relations as “living right and getting credit for it.” In a public relations program, the important thing is *what* you do—and if it's good, publicity will follow.

Only by serving others in the community will the Auxiliary be able to build the kind of public relations you want. If you serve well, your activities will be of interest to the community—not because it's something the Auxiliary is doing, but because of the people you help. Telling your story is a full time job. It means you must coordinate every program, every project, and constantly come up with new plans, new ways of serving.

Leadership implies at least three skills; first, the ability to make decisions; second, the capacity to get things done, and third, willingness to evaluate the results of such action. Other important qualities are: A philosophy about the Auxiliary, ability to delegate, flexibility to approach problems, ability to communicate, and the ability to visualize opportunity.

Perhaps the quality of greatest value to a leader is “the ability to get people to work hard, to work well, and to do so because they want to do so.”

Remember, leadership is a sort of relationship that is earned and accorded by others. It cannot be forced. Are you preparing your officers well by providing constant opportunity for participation and leadership? Someone once said, "Blessed is the leader who develops leaders while leading."

"A triumphal feast was scheduled in a village. And, to insure adequate liquid refreshments, each villager agreed to pour one bottle of his best wine into a great cask. "If I filled my bottle with water", reasoned one, "the dilution will be so slight, who will notice?"; but when the feast commenced, and the cask was tapped, nothing but water poured forth. Everybody in the village had figured alike: "My bit will not be missed!"

This fable points up a real problem in our auxiliaries. We need the membership and active participation of every eligible doctor's wife. Their bit is being missed! Of course, we ourselves must first believe in the program and purpose of the Auxiliary wholeheartedly, for the spirit of medical auxiliary service can be truly infectious, and the reward for a labor of love is simply the joy of service.

"There is destiny that makes us brothers
None goes his way alone;
All that we put into the lives of others
Comes back into our own."

The goal of the Woman's Auxiliary to the American Medical Association in their 50th year is 100,000 members. In Connecticut we are aiming for 1,000 members. Let's build on strength. The next year may very well be a most important one in medical legislation. We must unite to face this challenge.

BOOK REVIEWS

THE BEST OF LAW AND MEDICINE.

Reviewed by: J. ALFRED FABRO

"The Best of Law and Medicine—'68—'70" (AMA, $2.00) is a collection of articles reviewing the impact of existing legal rules and procedures on the practice of medicine in the United States. They appear regularly as the last pages of JAMA, written by the legal staff of the AMA. They are one evidence of the many excellent services and departments of the AMA that many physicians are not aware of.

It is impossible to review over 80 medicolegal articles, each dealing with a different subject. The table of contents includes the broad subjects of (1) medical liability, (2) hospital liability, (3) public policy and medicine, (4) licensure and disciplinary actions, (5) business problems related to medical practice, (6) mental health, (7) medical evidence, and a few miscellaneous subjects.

The articles have been written by lawyers who work full time in the AMA Legal Department, familiar with medical problems, and with the ability to write for physicians. The volume is well worth owning, individually and for a hospital library as a reference.

It gives a broad view of the problems physicians may encounter in their practice, with adequate references, and fortified with the knowledge that the reader may write to the AMA Legal Department for further information on any particular subject discussed.

I must mention a couple of caveats: (1) It is not written in text book style—with basic information in continuity and development of subject matter. Though there are the broad subjects mentioned above, each article is designed to stand by itself within 2 pages as published in the JAMA. (2) It is important and necessary for the physician to understand that explanation of the subject matter is done through utilization of actual cases from individual states. That being so, physicians must realize that the law being expounded in a legal case report reflects the law of that particular state. Even with the same set of facts, the law may be completely different in a different state.

But this does not detract from the value and purpose of the volume. It is intended to give a physician a "feel" for the law, for the subjects and problems he may encounter, with the writer reporting actual cases already adjudicated so as to inform the physician as to legal reasoning.

Most of the law related to the subjects discussed, especially in malpractice, is judge-made, case by case, state by state, in the tradition of the common law. To us physicians, trained to believe that science knows no boundaries, it is almost inconceivable that a dispute involving the same set of facts can result in contrary legal decisions in different states. But this still does not make such a compendium without value. It does serve to educate the physician about some of the pitfalls in his practice, and how courts have decided them.

Some of the specific legal problems included that are relatively new and of interest to physicians are: (1) Physicians' Liability for Staphylococcus Infections (2) Physician Risk in Blood Transfusion (3) Administration of Wrong Drugs (4) Liability for Penicillin Reactions (5) Use of Paramedical Personnel (6) The "Locality" Rule (7) Problems Associated with Intensive Care Units (8) Hospital Emergency Room Liability Cases (9) Due Process in Disciplinary Hearings (10) Liability for Acts of Physicians' Employees (11) Tax Deductions of Auto Expenses and of Traveling Expenses (12) Ownership of Physicians' Medical Records (13) Legal Aspects of Computerized Medical Records.

Its purchase is timely for Connecticut physicians. It can act as a supplement for the educational program the state medical society is beginning, in association with its new malpractice package deal with Aetna. Physicians need to be reminded that 80% of all malpractice occurs in hospitals; that not even the best trained physicians are immune to such suits; and that there is an appalling lack of real knowledge by physicians about even the basic facts about malpractice. Included in the compendium is a suggested curriculum for medical students, drawn up by the Committee on Medicolegal Problems of the AMA. It could well be used not only in our medical schools, but for hospital staffs and wherever there are training programs for internes and residents.

SYNOPSIS OF PEDIATRICS. Ed., 3. by James G. Hughes, M.D. The C. V. Mosby Co., 1971, 1113 pages with illustrations.

Reviewed by: WILLIAM E. LATTANZI

This is the 3rd edition of this book edited and partially written by Dr. Hughes, the Professor of Pediatrics at the Univ. of Tennessee. In what must be a fairly unique situation, all but three of the 27 contributors are faculty members of the Univ. of Tennessee College of Medicine.

Dr. Hughes in his preface to the first edition, states as one of his purposes the "explanation of the fundamental mechanisms of disease in an effort to bridge the gap between basic science and clinical pediatrics." It is this desire that differentiates this lengthy synopsis from other books in the field whose intent is more toward providing the reader with diagnostic possibilities and "cook book" treatment schedules. Some of the chapters, especially those on Growth & Development, Psychologic Aspects in Childhood, and Genetic Counseling, are outstanding in their clarity and practicality to those of us who deal with children and families. For the most part the chapters devoted to discussion of disease by systems are quite adequate. There are others, however, that are neither clear nor very useful to the sudent or the practicing physician. The many illustrations are well done and the appendix of normal values and drug dosages is well organized.

The book then, although excellent in parts, is somewhat uneven in its quality. This is probably inevitable in a synopsis that is struggling against becoming a full fledged text book, and whose contributors are drawn from one faculty of medicine.

news from the

Connecticut Regional Medical Program

Value Of Full Time Chiefs In Community Hospitals

Howard Levine, M.D.*

**Chief of Medicine, New Britain General Hospital.*

The Chief of Medicine furnished the beginning link between the New Britain General Hospital and the University of Connecticut Health Center.

The full-time Chief of Pediatrics, (Joseph Jurkoic, M.D. partially supported by CRMP) brought a marked change in the Department of Pediatrics after he took office in 1970. Through affiliation with U-Conn, the pediatrics residency training program is now being partly conducted at New Britain General Hospital. Fewer infants and children are transferred, or directly admitted, to outside hospitals. An effective educational program for pediatric attending physicians is now in effect. Four new pediatricians have been brought to the community; they were attracted by the hospital itself, by the developing relationship with the University of Connecticut Health Center, and by practice opportunities. An intensive care newborn nursery has been established. A neonatologist of the university staff is based at our hospital and has considerably benefitted the care of newborn infants. The nursing service is now better organized and more helpful. Plans are in effect for an outpatient well-baby clinic as well as an acute care out-patient clinic.

The Chairman of the University Department of Obstetrics and Gynecology also serves as Chief of the Ob-Gyn service at New Britain General Hospital and is based at the hospital. A university gynecologist-oncologist is serving part-time at our hospital.

It is striking to note that the Surgical Department, previously rated as offering the strongest residency program has, within two years, lost that rating. This is the only residency not headed by a full-time chief. The attending staff acknowledge the need for a full-time Chief of Surgery. Active recruitment is underway and New Britain General Hospital welcomes CRMP partial support.

The presence of students at this hospital at each level of medical school training has offered stimulation to the house staff and attending staff. The University relationship has further brought to the community hospital subspecialists in areas of need, for example, endocrinology, infectious disease, rheumatology, nephrology, and to some extent, hematology. These subspecialists come not only in direct response to the hospital's teaching program but also to provide consultative services for the practicing staff.

Weekly bedside rounds are conducted by a U-Conn professor. The total input of the CRMP-supported University staff in the Department of Medicine averages 6-10 hours per week. The University input on Ob-Gyn and Pediatrics is greater. Having the New Britain General Hospital Chief of Service on the University Faculty permits direct communication between the community hospital and the University. There has also been rotation of the University interns and residents for an elective in cardiology and intensive care unit at this hospital.

We look forward to closer affiliation and to eventual integration of a University and Community Hospital program in the area of medicine. The educational resources of the University are needed to more fully develop all programs; closed circuit TV and audiovisual aids, such as films, which can be based at the University but beamed by TV to local hospitals, are an exciting future possibiliity.

With the improvement in quality of medical care and better utilization of hospitals—which we believe is already apparent in our institution—there should be an overall decrease in the cost of medical care in the community; this would more than justify the sum needed to support the Chiefs of Service. We recognize that it is necessary to develop new methods of evaluating patient care. In the meantime peer review of medical records by medical staff, both full-time and practicing physicians, indicates that there has been such an improvement in patient care.

Connecticut Medicine

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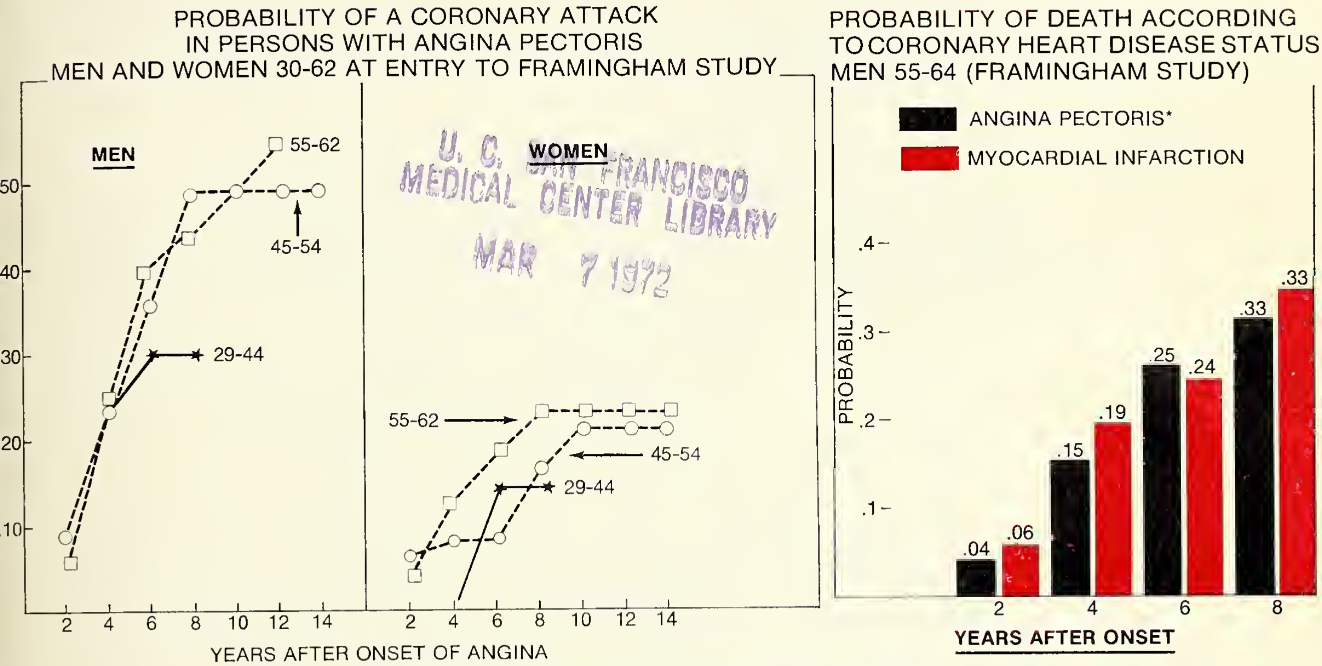

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APRIL 25, 26, 27, 1972—HARTFORD HILTON HOTEL, HARTFORD

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(urethritis, cervicitis, proctitis when due
to susceptible strains of N. gonorrhoeae)

Sterile Trobicin®
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An aminocyclitol antibiotic active *in vitro* against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive *in vitro* studies have shown no cross resistance of *N. gonorrhoeae* between Trobicin and penicillin.

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Contraindications: Contraindicated in patients previously found hypersensitive to Trobicin. Not indicated for the treatment of syphilis.

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Warnings: Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance of *N. gonorrhaeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia.
During multiple-dase subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemo-

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Active against most strains of Neisseria gonorrhoeae in vitro (M.I.C. 7.5-20 mcg/ml)

A single two-gram injection produces peak serum concentrations averaging about 100 mcg/ml in one hour (average serum concentrations of 15 mcg/ml present 8 hours after dosing)

Note: Antibiotics used in high doses for short periods of time to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Since the treatment of syphilis demands prolonged therapy with any effective antibiotic, and since Trobicin is not indicated in the treatment of syphilis, patients being treated for gonorrhea should be closely observed clinically. Monthly serological follow-up for at least 3 months should be instituted if the diagnosis of syphilis is suspected. Trobicin is contraindicated in patients previously found hypersensitive to it.

*Data compiled from reports of 14 investigators. **Diagnosis was confirmed by cultural identification of *N. gonorrhoeae* on Thayer-Martin media in all patients. Criteria for cure: negative culture after at least 2 days post-treatment in males and at least 7 days post-treatment in females. Any positive culture obtained post-treatment was considered evidence of treatment failure even though the follow-up period might have been less than the periods cited above under "criteria for cure" except when the investigator determined that reinfection through additional sexual contacts was likely. Such cases were judged to be reinfections rather than relapses or failures. These cases were regarded as non-evaluatable and were not included. JA72 1848-6

globin; hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25°C and use within 24 hours after reconstitution with diluent.
Male—single 2 gram dose (5 ml) intramuscularly. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.
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180th ANNUAL MEETING
CONNECTICUT STATE MEDICAL SOCIETY

Hartford Hilton Hotel
10 Ford Street, Hartford, Connecticut

April 25, 26, 27, 1972

PRELIMINARY PROGRAM

TUESDAY, APRIL 25

ANNUAL MEETING OF THE HOUSE OF DELEGATES

TERRACE ROOM —::— MEZZANINE

Presiding: Kenneth F. Brandon, Hartford, Connecticut, Speaker of the House
Timothy F. Nolan, Greenwich, Connecticut, Vice-Speaker of the House

The 1972 Annual Meeting of the House of Delegates is scheduled to be held in the Terrace Room of the Hartford Hilton Hotel, Hartford, on Tuesday, April 25, commencing at 8:30 A.M. Following luncheon, the House will reconvene to complete its business.

ROUND TABLE DISCUSSIONS

Members of the Society are invited and encouraged to participate in the Round Table Discussion or "Learning Panels". Four of these panels will be held on Wednesday, April 26, and four on Thursday, April, 27. The subject, time and place for each is published in the Program that follows. The respective "Learning Panels" will be chaired by experienced physicians who will lead their groups, of not more than 15 participants, through in-depth examination of the topics assigned. Active participation in the group discussion will be limited to members who have pre-registered. (Registration Forms will be mailed to members with the Program of the meeting). Members who have not pre-registered will be welcome to attend the Panels as observers only, within the limits of available seating capacity.

WEDNESDAY APRIL 26

SCIENTIFIC PROGRAM

MORNING SESSIONS

8:30 Registration—Mezzaine

ROUND TABLE DISCUSSIONS

8:45-10:00 Fourth Floor in Rooms Designated

Pharmacological Problems of the Pregnant State—Room 412
Group Leader: Jack N. Blechner, New Britain, Connecticut

Laboratory Problems Resulting From the Use of Common Drugs—Room 416
Group Leader: James E. O'Brien, Hartford, Connecticut

Pharmacological Considerations In Renal Disease—Room 420
Group Leader: George F. Thornton, Waterbury, Connecticut

Pharmacological Problems of Anti-Arrythmic Drugs—Room 424
Group Leader: Martin J. Krauthamer, Darien, Connecticut

10:00 Intermission to Visit Exhibits

TERRACE ROOM

10:25 Opening Remarks
Michael J. Esposito, Meriden, Connecticut, Chairman, CSMS Committee on Program of Scientific Assembly

SYMPOSIUM ON THE NEW CLINICAL PHARMACOLOGY

Presiding: Robert J. Levine, New Haven, Connecticut

10:30 What You Need To Know—Basic Concepts
Bert N. LaDu, New York City

11:15 Practical Aspects of Drug Interactions
Jan Koch-Weser, Boston, Massachusetts

12:00 Panel Discussion
Moderator: William F. Eckhardt, Jr., New Canaan, Connecticut
Panelists: Bert N. LaDu, Jan Koch-Weser, Robert J. Levine

12:30 Intermission to Visit Exhibits

1:00 Luncheon—Cities Rooms

AFTERNOON SESSION

TERRACE ROOM

Presiding: James E. O'Brien, Hartford, Connecticut

2:00 Clinical Pharmacology and Problems Created by Newer Diuretic Drugs
Paul J. Cannon, New York City

2:40 Current Therapy of Hypertension
Robert W. Wilkins, Boston, Massachusetts

3:30 Intermission to Visit Exhibits
Section Meetings

EVENING PROGRAM

6:15 Reception—Mezzanine

7:00 Annual Dinner of the Society
Inauguration of the President

THURSDAY, APRIL 27

SCIENTIFIC PROGRAM

MORNING SESSIONS

8:30 Registration—Mezzanine

ROUND TABLE DISCUSSIONS

8:45-10:00 Fourth Floor in Rooms Designated

Pharmacological Problems of the Newborn—Room 412
Group Leader: Robert L. Harris, West Hartford, Connecticut

Pharmacological Problems of Drug Abuse—Room 416
Group Leader: Robert A. Kramer, Hartford, Connecticut

Clinical Pharmacology of the Common Anti-Neoplastic Drugs—Room 420
Group Leader: Ronald C. DeConti, New Haven, Connecticut

Current Status of Oral Hypoglycemic Agents—Room 424
Group Leader: Philip Felig, New Haven, Connecticut

10:00 Intermission to Visit Exhibits

TERRACE ROOM

SYMPOSIUM ON THE RHEUMATOID STATE

Presiding: Naomi Rothfield, Hartford, Connecticut

10:30 What's Wrong in Rheumatic Disease—Basic Mechanisms
Gerald Weissmann, New York City

11:15 Anti-Inflammatory Drugs—Clinical Usage
Thomas G. Kantor, New York City

12:00 Panel Discussion
Moderator: Howard Levine, New Britain, Connecticut
Panelists: Gerald Weissmann, Thomas G. Kantor, Naomi Rothfield

12:30 Intermission to Visit Exhibits

AFTERNOON SESSION

TERRACE ROOM

Program to be Arranged with Connecticut Society of American Board Surgeons

PRESIDENT'S PAGE

It would seem only natural in an era of extraordinary advancement in scientific knowledge and technology that there also would be rapid changes in mores, customs, and values. In the field of medicine the new drugs and vaccines, diagnostic tests, therapeutic instruments and surgical techniques have given rise to control of infectious disease, prenatal diagnosis of genetically determined disease, pacemakers, and organ transplants to name only a few obvious examples. These new practices have given rise to a change in outlook and perspective in certain fields of practice.

Accompanying this progress in man's control over his afflictions are, of course, new problems. We now have to deal with more people in the older age groups who are subject to senescence. This leads to further research into the causes of arteriosclerosis and to a study of the process of aging itself. Premarital counseling and the decision as to whether an abortion is necessary or acceptable are responsibilities resulting from knowledge of inherited disease. How far to go in efforts of resuscitation, and how to allocate kidney dialysis and transplant facilities pose very serious and searching questions.

The general area involved by these questions comes under the heading of *Ethics*. It is not limited to interrelationships between doctors. Ethics are involved in doctor-patient and doctor-family relationships. It is necessary to practice this form daily and constantly to maintain patient confidence. The ethical questions involved in treating patients on mechanical respiratory and cardiac pacers and when to take out an organ for transplant are more difficult because of their unfamiliarity. The answer to most of these new decisions is to get an additional opinion from other colleagues; share the judgment and responsibility.

Leon R. Kass, executive secretary, Committee on the Life Science and Social Policy, National Research Council, in an article in *Science* (November 19, 1971, 174:4011, page 779) writes on "The New Biology: What Price Relieving Man's Estate?" He brings up many new scientific discoveries and points out the ethical dilemmas presented in following them to their human applications.

It is in consultation and discussion that the medical profession can deal with new problems of ethics as they arise. We should not fear the possible and even likely development of more mind altering drugs, nor decisions as to when to cease resuscitation, nor when to remove an organ for transplant. We must not neglect the wisdom of the clergy and the pragmatism of the lawyers in approaching the ethical questions of the future. With the confidence of the patient and his family, backed by an educated, understanding public, and above all with a humanistic attitude toward the future of society, there should be no doubt of finding a proper ethical solution to the most far reaching of scientific developments.

Frederick C. Weber, Jr., M.D.

Special Report

A Comparison of Six Major Proposals for National Health Insurance

John M. Glasgow, Ph.D.

A current topic of major economic and political significance is the future pattern of the financing of the cost of health care in the United States. In the last two years, a number of legislative proposals have been introduced in the Congress which called for the institution of some form of national health insurance system or for the development of a national health program. These proposals utilize a variety of approaches, contain differing benefit patterns, have diverse populations included in their coverage, employ varied financing and payment mechanisms, and propose widely varied impacts on the present system for the organization and delivery of health care. Consequently, it is difficult to keep separate the major provisions of the various proposals.

To assist in the comparison of the six principal proposals currently being discussed, the following summary of the major provisions of each has been developed. These six proposals are the Health Security bill, the Javits plan, the Nixon Administration's National Health Insurance Partnership program, the Ameriplan, the Medicredit plan, and the Healthcare plan. The summaries include the major features involved in the general approach, the population covered, the benefit pattern provided, the financing and payment mechanism utilized, and the health system changes envisioned. It does not include cost estimates since in some cases the details on benefits and eligible populations are not available. Even where the proposed costs of a plan are provided by its sponsor these costs are often questioned by others. Finally, given the differences in program approach and impact, cost estimates would lack comparability even if known.

A. HEALTH SECURITY ACT OF 1971

Introduced by Senator Edward Kennedy (D-Mass.) as S.3 and as H.R. 22 by Representative Griffiths (D-Mich.), sponsored by Committee for National Health Insurance, AFL-CIO, UAW, and other labor groups, the measure is based on the concept of a comprehensive, compulsory health insurance program as an integral part of the national social insurance system.

Population Coverage

All U.S. Citizens, plus aliens admitted as a permanent resident or admitted for employment and employed within U.S., while within the U.S. Certain non-resident aliens could be included under reciprocal and "buy-in" agreements.

Benefit Pattern

Comprehensive personal health care with limitations on nursing home care, psychiatric care, dental care, and drugs. Intent is to remove most limitations over time. No cut-off dates, no coinsurance, no deductibles, no waiting periods. Benefits would not take effect for two years after law enacted.

Administration

Health program administered by 5 member Health Security Board within DHEW. National Advisory Council, including consumer representatives to assist in development of policy. Field administration by regional, subregional and local units with strong discretionary power.

Financing

Employer, employee, self-employed and federal government share in costs: 50% from general Federal Tax revenues; 36% from 3.5% tax on employers payrolls; 12% from 1% tax on wages up to $15,000/yr.; 2% from 2.5% tax on self-employed income up to $15,000/yr. Employee share may be paid by employer if called for by union negotiated or employer-employee arrangements.

Payment Mechanism

Given amount of money will be allocated for health expenditures annually. Board will allocate funds to the several regions for further subdivision

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among categories of services in health subareas. Of funds in a service area, amount sufficient to pay physicians receiving salaries and for the professional services component of institutional budgets are first priority expenditure. Residual of funds divided by population to compute percapita payment in each service category. Hospitals and other institutional providers will be paid on the basis of approved prospective budgets. Independent practitioners may be paid by various methods which they may elect: by fee-for-service, by capitation payments, or in some cases by retainers, stipends, or a combination of such methods. Comprehensive health service organizations may be paid by capitation, or by a combination of capitation and methods applicable to payments to hospitals and other institutional providers. Other independent providers will be paid by methods adapted to their special characteristics.

Effects on Health Care Delivery System

Provides financial levers to restructure health delivery system. Strong emphasis on development of group practice programs and preventive health measures. Substantial grants available to develop innovative health systems and assure availability of care in local communities. High national standards for participating providers and facilities, including Board standards for major surgery and other specialist services; requirements for continuing medical education, national minimum licensure standards. Financial support provided for systems which efficiently organize and utilize all levels of medical manpower. Special funds available to subsidize the training and initial utilization of new types of professional manpower and paraprofessional personnel with special emphasis on programs for training poor or minority groups. Special support for location of increased health personnel in urban and rural poverty areas. Prospective budgeting for institutional services. Consumer participation in health care system encouraged.

B. NATIONAL HEALTH INSURANCE AND HEALTH IMPROVEMENT ACT OF 1971

Introduced by Senator Javits (R-N.Y.) as S. 836, this bill would expand Medicare program to the general population on a phased basis.

Population Coverage

Program phased in covering first the disabled, poor and unemployed before extension to the generaral population, including citizens and aliens admitted for permanent residence, on July 1, 1974.

Benefit Pattern

Benefits would be same as present Medicare program (part A & B), including limitations, deductions, and coinsurance features, with phased addition of a drug benefit limited to certain long-term maintenance drugs with $1 copayment per prescription; annual physician exam and eye, ear, and routine dental care to those under 8; and, assumption of part B premium.

Administration

Private insurance companies act as fiscal agents for the government plan and as insurers and underwriters for private plans. National standards with state monitoring of insurance companies. Option exists for federally chartered corporation in cases where intermediaries' management is inefficient or uneconomical.

Financing

Payroll tax on employees wages up to $15,000, employer tax based on total payroll, and tax on self-employed would cover two-thirds of cost. Federal share (one-third) from general revenues pays for cost of including nonworking population.

Payment Mechanism

Transitional use of present Medicare payment system (based on reasonable cost or charges). Future method to be designed to control cost and utilization and improve organization of medical services. Payments to approved comprehensive health service systems may be on basis of reasonable costs or predetermined capitation amount.

Effect on Health Care Delivery System

Provides financial (including share in savings) and technical assistance to comprehensive health service systems. Increased government financing of capital hospital construction. Board standards for major surgery and other specialist services, requirements for continuing medical education, national minimum licensure standards required to assure quality. Encourage better utilization of manpower through comprehensive group practice. Establishes concept of appropriate rather than reasonable reimbursement, based on worth of services when efficiently delivered.

C. NATIONAL HEALTH INSURANCE PARTNERSHIP

Proposed by the Nixon Administration, introduced as S. 1623 by Senator Bennett (R-Utah) and, with modifications, as H.R. 7741 by Representative Byrnes (R-Wis.). A three part approach involving

(1) mandatory employer financed health insurance for their employees; (2) federally financed health insurance for poor families; and (3) retention of Medicare for those over 65.

Population Coverage

Mandatory employer provided plans should cover all but the self-employed, federal employees, and those outside the labor force. These would be covered by existing plans; through purchase of insurance at group rates from state pools of private insurers; or, in the case of the poor, by federally subsidized plan.

Benefit Pattern

Minimum plan which employers could buy would provide a range of hospital, ambulatory, and preventive services (including catastrophic illness, maternity and child care coverage) which meet federal standards. Medicaid would be replaced by a Family Health Insurance Plan with total federal financing of part or all of cost of private insurance or capitation charge of prepaid group practice. Benefits under employer provided plan are not subject to limits; those provided to poor under FHIP are. Part A & B of Medicare would be combined and Part B premium dropped. Benefits could be obtained either from HMO or independent providers. Beneficiary responsible for deductibles and coinsurance, amount would vary with income of eligible family in case of FHIP. Coinsurance and deductibles would be waived for all after individual receives $5,000 of covered services in a benefit year.

Administration

Private insurance companies, with federal regulation of their organization and costs, would administer employer provided plans. FHIP would be a federally administered program.

Financing

The employer provided benefit plan would be paid for primarily by the employer with payments deductible for income tax purposes. Changed Medicare program financed by increases in both the tax rate and the base taxable under Social Security. The FHIP would be financed out of general revenues. Tax credits given for private purchase of insurance plans.

Payment Mechanism

Predetermined capitation to HMO's. Present methods under private insurance in other cases subject to federal review and standards criteria.

Effects on Health Care Delivery System

Major financial push to development of prepaid group practice concept through provision of planning grants and loan guarantees. Financial support for training and utilization of new types of health manpower or increased supply, with special emphasis on increased opportunities for disadvantaged students. Funds for the development of new organizational forms such as consortia and area health education centers. Special support to encourage location of physicians in areas where there are few or no M.D.'s.

D. AMERIPLAN

Sponsored by the American Hospital Association, the program calls for the utilization of all existing sources of funds to finance payments to Health Care Corporation which would provide comprehensive care to defined populations and geographic areas. Medicare and Medicaid would be eliminated.

Population Coverage

Health Care Corporations (400), under legislation to be enacted by the Federal Government, would be established in every geographic area to assure that all citizens have access to care.

Benefit Pattern

Three major benefits packages would be offered to Corporation members—health maintenance and catastrophic illness, standard benefits, and supplemental benefits. Standard benefits, uniform for all covered persons, subject to limitations and coinsurance, would include primary, speciality, restorative, and health related custodial care. Health maintenance and catastrophic illness package, in effect only after standard and supplemental benefits exhausted and if beneficiary registered with Corporation, includes well baby immunizations, multiphasic screening, and certain other preventive care benefits. Various packages of supplemental benefits (not yet specified) would be available.

Administration

Federal legislation will be required to implement Ameriplan through the establishment of a National Health Commission with the responsibility for adopting regulations to create uniform benefit packages and state the scope, standards of quality, and comprehensiveness of health services. This Federal law would then motivate states to enact legislation, by a specified date, establishing health commissions to regulate Health Care Corporations and be responsible for their approval and operation. Health Care Corporations developed through agreement or merger of existing provider organizations; as a local government authority; or as a private corporation.

Financing

Federal subsidy of the health maintenance and catastrophic illness package for the poor, and in part for the near-poor through general tax revenues. Aged and all others covered by Social Security Taxes. Standard benefits directly purchased by those under age 65; benefits purchased for poor and near-poor by Federal Government from general tax revenues; aged included through Social Security. Supplemental benefits available through prepayment plans or private insurance to those "able to pay".

Payment Mechanism

Maintenance benefits paid for on a capitation basis. All other services paid for on basis of prospectively determined rates as approved by the State Health Commission. Within Health Care Corporations, physicians could elect method of payment.

Effects on Health Care System

Attempts to unite all health resources in a given geographical area under one organization. Strong emphasis on ambulatory services. Health Care Organization responsible for establishment, and expansion into office practice, of peer review and other mechanisms for evaluation of quality of care; for the function of licensing health personnel in accordance with national standards to be established; develop incentives to assure use of most efficient and appropriate services; and, inservice education and training of its health manpower.

E. HEALTH CARE INSURANCE ACT OF 1971 (MEDICREDIT)

Sponsored by the American Medical Association and introduced as S. 987 by Senator Hansen (R-Wyo.) and Representative Broyhill (R-Va.), the bill would provide tax credits for private health insurance coverage scaled to income tax liability with lowest income groups provided free insurance. Tax credit would include 100 percent of premium charges for catastrophic illness insurance. Medicare would remain intact for aged; Medicaid would be eliminated.

Population Coverage

Total population would be eligible to purchase private plans. Government would pay full premium for low income groups having no income tax liability with varying amount of premium cost for other poor.

Benefit Pattern

Includes two benefit packages. Basic policy would offer 60 days in-patient hospital service plus full range of outpatient and physicians services in hospital, home, or office. Catastrophic plan would include hospital, extended care facility, in-patient drugs, blood, appliance and other services. Patient responsible for deductibles and co-insurance plus corridor between basic coverage and catastrophic illness coverage.

Administration

Medicare continues to be handled by intermediaries; private insurers handle their own participants under age 65. Federal Health Insurance Advisory Board would establish standards for insurance carriers and develop programs to maintain quality health care and effective use of health resources. Advisory Board would be appointed by President with Senate consent.

Financing

Income tax credits for cost of private insurance. Percentage of allowed credit based on personal income tax liability. Tax credit ranges from 100% for those with no tax liability to 10% for tax liability in excess of $891. Those eligible for full payment of premium by Federal government would be issued a certificate enabling purchase of private insurance plan. Others could elect between tax credit or a certificate.

Payment Mechanism

Continuation of present methods under private insurance.

Effects on Health Care System

No changes in present system proposed although a peer review mechanism is to be submitted as a separate legislative proposal.

F. NATIONAL HEALTH-CARE ACT

Sponsored by the Health Insurance Association of America and introduced by Representative Burleson (D-Tex.) as H.R. 4349 and Senator McIntyre (D-N.H.), the Health Care plan would provide a comprehensive insurance program based on the concept of voluntary private insurance with cost of package subsidized for poor and near-poor. It would utilize federal income tax incentives to help assure maintenance of benefit levels. Medicare would be unaffected; Medicaid would be eliminated.

Population Coverage

Total population would be eligible to purchase a standard benefit package, but enrollment would be voluntary. Qualified State Health Care Plans would be established to provide same coverage for low-income and "uninsurable" groups.

Benefit Pattern

Two benefit packages included. Private groups and individuals could purchase a Minimum Standards Health Care Benefits package with includes ambulatory and preventive care benefits. State pool benefits for poor and near-poor include all MSHC benefits plus dental care for those under 19, maternity care, family planning services and supplies, and rehabilitation services. The scope of benefits included in privately purchased MSHC plans would increase in phases until raised to state pool levels. Plans subject to limitations, deductibles, and coinsurance. Aggregate amount of co-payment limited to an annual dollar amount or given percentage of family income. Coordination of benefit payment to avoid duplication of coverage.

Administration

Programs administered by private insurance companies. One carrier or a group of carriers would be chosen by state to administer the State Health Care Plan for poor and non-insurables.

Financing

Federal and State funds to purchase benefits for poor and near-poor on basis of income level related variable subsidy. Others buy own policy with income tax credit given for full cost of those policies which meet the national benefit minimum. Lesser benefit policies receive 50% tax credit. Expenses which experience demonstrates to be overutilized would be subject to copayment. The aggregate limit on copayment would be related to family income.

Payment Mechanism

Continuation of present methods under private insurance.

Effects on Health Care System

No direct effect built into the insurance program except for emphasis on ambulatory and preventive care. Assume program to be instituted in conjunction with other actions by Federal Government: continuation of health manpower programs; loans and grants to increase health manpower and direct location to areas of greatest need; increased hospital construction grant and low guarantees and expansion of program to include ambulatory care centers; imposition of cost and quality controls, including utilization and peer review; standard accounting; increased support for, and expanded duties of comprehensive health planning agencies to include establishment of community need priorities and determination of need for tax supported services.

From the Pamphlet Shelf

OLD KING COLD. As one in a series of pamphlets prepared by the AMA's MD-Patient Information Service, OLD KING COLD covers the subtopics: what causes colds, how to catch a cold, and what to do for a cold.

The information, related in a rather humorous fashion, emphasizes that this trouble maker costs the United States over $5 billion annually in lost wages, lost production, and medical expenses.

Single copies are available by contacting Leonard R. Tomat, Assistant Executive Director, CSMS, 160 St. Ronan Street, New Haven, Connecticut 06511.

The Relationship of Incidence of Cervical Cancer and Socioeconomic Status in Seven Cities, 1959-1964

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This study, carried on by the chronic disease control section of the Connecticut State Department of Health, and the Department of Rural Sociology of the University of Connecticut, focused on the relationship between the incidence of cervical cancer and the socioeconomic level of census tract areas in each of seven Connecticut cities. Data for all the cities combined were also utilized to analyze the relationship between cancer incidence and socioeconomic status which characterizes urban areas as a class.

It has been found in the past that the magnitude of some social phenomena increase as socioeconomic status decreases. Fertility rates, mental disorders, delinquency, suicide, and overall mortality vary in this manner.[1] Cancer of the cervix has been reported to be more prevalent in persons of low socioeconomic areas.[2] This investigation relates the rate of occurrence of cervical cancer to socioeconomic status in Connecticut. Because cancer of the cervix can be detected in its non-invasive curable stage (carcinoma in situ) by use of the Papanicolaou smear, such investigation was justified in that it might assist in eradicating from Connecticut the less curable invasive cervical cancer by indicating in what areas screening procedures, clinics, and cancer education programs are most needed.

Data and Methods

The analytical framework employed in this study is "Social Area Analysis." A measure of socioeconomic status of geographic areas put forth by Stockwell and Shea was used.[3] It consists of three scores for each area based upon (1) the occupational level, (2) the educational level, and, (3) the income level of the area's population. The three scores are standardized and the arithmetic mean of the three is taken as the area's social rank score. Stockwell and Nagi computed social rank scores for the census tracts of the inner cities of Connecticut's seven large metropolitan areas.[4] They combined census tracts with similar social rank scores into social rank areas referred to as SRA's. This allowed the contrasting of large sections of cities with respect to social and demographic phenomena.

The present study related the incidence of cervical cancer to the social rank areas delineated by Stockwell and Nagi. Included were all cases of cervical cancer diagnosed during the six year period 1959-1964 in women residing in these areas. There was a total of 909 tumors of which 460 were in situ and 449 invasive. These cases were reported by hospital tumor registries to the Connecticut Tumor Registry where all pertinent information including age, street and city of residence, site of tumor, and stage of disease was coded from case abstracts. The street and city of residence were utilized for allocation of cases to the proper social rank areas. The population bases used in computing observed incidence rates were the female populations in each five year age group of each SRA as enumerated in the 1960 United States Census of Population.

Incidence rates for each SRA were age-standardized by the method of indirect standardization. This method standardizes rates by applying standard incidence rates to each female five year age group. The resulting expected number of cancer cases is compared with the observed or actual number of cancer cases in each age group and a correction factor is applied to standardize the observed or actual incidence rate of cancer. Age specific incidence rates of cervical cancer for the entire state of Connecticut in 1960 were employed as the standard rates.

Three types of age standardized incidence rates

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were computed for each social rank area, SRA, of the seven cities—the rate for in situ (non-invasive) cervical cancer, that for invasive cancer (localized, regional and remote), and a total rate (in situ and invasive tumors combined). These rates were also calculated for like SRA's of the seven cities combined.

Age standardization eliminates the effects of age by comparing the actual incidence rate characterizing a population to the rate which obtains in some population with a known age computation (the standard population). When a series of rates are adjusted to the same standard population they are directly comparable.

It must be noted that the age standardized rates are not absolute measures of the level of disease incidence and should not be treated as such. Rather than reflect the true incidence they present the incidence in a given population relative to its level in the standard population and thus can be compared only with other rates which have been standardized by the same method.

Because annual rates might in some cases have been small, six year rates have been employed. They present the experience of each population over the six year period.

Results

First to be considered is the relationship between the incidence of cervical cancer (in situ and invasive) and socioeconomic status based on the data from all of the seven metropolitan areas combined. Table 1 shows that the incidence of cervical cancer is inversely related to socioeconomic status. The lower the socioeconomic status of an area, the higher the incidence of cervical cancer. This inverse relationship is also seen for in situ and invasive cervical cancer taken separately. In situ lesions make up a somewhat greater proportion of tumors in the upper socioeconomic level, SRA I, than in the lower, SRA V, whereas the proportion of invasive rate is higher in the low socioeconomic area, SRA V.

Table 2 presents the data for the seven cities individually. It is noted that although there is some variation in patterns the age standardized incidence rates of in situ and invasive cervical cancer combined are inversely related to socioeconomic status in all except city F. That is, the incidence of cervical cancer is lowest in the high socioeconomic areas (SRA I) and highest in the low socioeconomic area (SRA IV and V). The inverse relationship appears strongest in cities B, C, and E. City A shows

TABLE 2

AGE STANDARDIZED INCIDENCE RATES OF CERVICAL CANCER AMONG WOMEN 15 YEARS OF AGE AND OLDER IN CONNECTICUT'S MAJOR METROPOLITAN AREAS BY SOCIAL RANK AREAS,[1] (1959-1964)

	Total Metropolitan Areas[2]	*City*[3] *A*	*City B*	*City C*	*City D*	*City E*	*City F*	*City G*
Total	3.26	4.70	4.25	2.83	2.26	2.94	2.98	1.83
SRA I[4]	1.98	—*	2.48	1.49	1.04	1.86	2.87	—*
SRA II	2.31	3.90	2.93	1.65	1.12	1.98	2.64	1.05
SRA III	3.33	4.08	4.09	2.91	2.78	3.94	3.59	1.86
SRA IV	3.93	6.06	5.57	3.11	2.13	4.30	2.98	2.23
SRA V	4.86	5.65	6.35	4.47	3.43	—*	—*	2.13

* Rates are not shown where data is insufficient to merit computations or no census tracts are contained in a specific social rank area.

[1] The Indirect Method of Standardization was used in this analysis. Rates shown *should not be compared* to rates from other sources because of the unique methods used in their calculation which are described in the text of this report.

[2] The metropolitan Areas are those utilized in a report by Stockwell and Nagi, "The Social Areas of Metropolitan Connecticut," Storrs Agricultural Experiment Station Bulletin #404, (March, 1968). They do not include all of the areas included in the census definition of SMSA's in Connecticut.

[3] Cities have not been identified by name in order to preserve their anonymity.

[4] The Social Rank Areas used are those developed by Stockwell and Nagi in the Storrs Agricultural Experiment Station Bulletin #404 (March, 1968).

TABLE 1

AGE STANDARDIZED INCIDENCE RATES AND THEIR PROPORTIONS, BY SOCIAL RANK AREA, FOR SEVEN CITIES COMBINED. CONNECTICUT 1959-1964

	Total Cervical Cancer Incidence Rate					*In Situ Rate*					*Invasive Rate*				
	SRA I	*SRA II*	*SRA III*	*SRA IV*	*SRA V*	*SRA I*	*SRA II*	*SRA III*	*SRA IV*	*SRA V*	*SRA I*	*SRA II*	*SRA III*	*SRA IV*	*SRA V*
Total Rate[1]	2.0	2.3	3.3	3.9	4.9	1.0	1.2	1.7	1.9	2.3	0.9	1.1	1.6	2.0	2.5
proportion of total rate	—	—	—	—	—	.52	.50	.52	.49	.48	.48	.50	.48	.51	.52

[1] Due to rounding the sum of the in situ rate of a given SRA and the corresponding invasive rate will not always equal the total rate.

a strong relationship although the rate, after a consistent rise, declines in SRA V. City G also shows a decline in SRA V, while cities D and E show dips in SRA IV. A total lack of pattern is seen for city F whose rates for SRA I, II and IV vary but little while that for SRA III is noticeably higher.

TABLE 3

AGE STANDARDIZED INCIDENCE RATES OF IN SITU CERVICAL CANCER AMONG WOMEN 15 YEARS OF AGE AND OLDER IN THE CENTRAL CITIES OF CONNECTICUT'S MAJOR METROPOLITAN AREAS BY SOCIAL RANK AREAS,[1] 1959-1964

	Total Metropolitan Areas[2]	*City*[3] *A*	*City B*	*City C*	*City D*	*City E*	*City F*	*City G*
Total	1.65	2.57	2.49	1.40	0.72	1.60	1.31	0.85
SRA I[4]	1.04	—*	1.49	0.74	0.15	1.12	1.66	—*
SRA II	1.16	1.84	1.55	1.00	0.24	1.32	1.28	0.52
SRA III	1.74	2.36	2.66	1.49	1.04	2.02	1.12	0.91
SRA IV	1.92	2.90	3.28	1.49	0.75	1.98	0.89	1.06
SRA V	2.32	3.45	3.37	1.49	0.90	—*	—*	0.43

* Rates are not shown where data is insufficient to merit computations or no census tracts are contained in a specific social rank area.

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[3] Cities have not been identified by name in order to preserve their anonymity.

[4] The Social Rank Areas used are those developed by Stockwell and Nagi in the Storrs Agricultural Experiment Station Bulletin #404, (March, 1968).

Table 3 presents the in situ rates. When broken down into the seven metropolitan areas the inverse relationship of incidence to socioeconomic area evident when all cities were combined continues for the most part. Cities A and B show strong inverse relationships. Though the inverse tendency is also evident in cities C, D, E and G the latter city has its highest rate at SRA IV while in C, D, and E it reaches its height at SRA III and remains constant or declines. City F, on the contrary, shows a direct relationship of in situ cervical cancer to socioeconomic area with the highest rate found in SRA I and a steady decline to SRA IV.

In Table 4 the rates for invasive cervical tumors vary inversely to social rank area for cities B, C, D, E, and G. In city F the invasive rates increase through SRA IV and decline slightly at SRA V. An irregular pattern is seen in City A with decreasing rates noted in SRA III and V. The invasive rate for City A is the only one markedly higher at 2.12 per 1,000 female population than that of all cities combined, 1.61, and that for city G is noticeably lower at 0.98.

TABLE 4

AGE STANDARDIZED INCIDENCE RATES OF INVASIVE (INCLUDING LOCALIZED) CERVICAL CANCER AMONG WOMEN 15 YEARS OF AGE AND OLDER IN THE CENTRAL CITIES OF CONNECTICUT'S MAJOR METROPOLITAN AREAS BY SOCIAL RANK AREAS,[1] (1959-1964)

	Total Metropolitan Areas[2]	*City*[3] *A*	*City B*	*City C*	*City D*	*City E*	*City F*	*City G*
Total	1.61	2.12	1.77	1.44	1.53	1.34	1.67	0.98
SRA I[4]	0.95	—*	1.00	0.74	0.90	0.75	1.21	—*
SRA II	1.14	2.06	1.37	0.66	0.87	0.66	1.36	0.52
SRA III	1.59	1.72	1.43	1.42	1.74	1.90	2.48	0.96
SRA IV	2.02	3.16	2.28	1.62	1.39	2.32	2.08	1.17
SRA V	2.53	2.20	2.98	2.98	2.53	—*	—*	1.71

* Rates are not shown where data is insufficient to merit computations or no census tracts are contained in a specific social rank area.

[1] The Indirect Method of Standardization was used in this analysis. Rates shown *should not be compared* to rates from other sources because of the unique methods used in their calculation which are described in the text of this report.

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[2] Cities have not been identified by name in order to preserve their anonymity.

[4] The Social Rank Areas used are those developed by Stockwell and Nagi in the Storrs Agricultural Experiment Station Bulletin #404, (March, 1968).

Table 5 presents the total, in situ and invasive rates for each of the central cities of the seven metropolitan areas, arranged in decreasing order

TABLE 5

AGE STANDARDIZED INCIDENCE RATES[1] OF CERVICAL CANCER IN SEVEN METROPOLITAN AREAS, CONNECTICUT, 1959-1964

City	*Total Incidence Rate*	*In Situ Rate*	*Invasive Rate*[2]
A	4.70[3]	2.57	2.12
B	4.25	2.49	1.77
C	2.83	1.40	1.44
D	2.26	0.72	1.53
E	2.94	1.60	1.34
F	2.98	1.31	1.67
G	1.83	0.85	0.98

[1] Females aged 15 years and over per 1,000 female population.

[2] Invasive rate contains localized, regional and remote tumors.

[3] Due to rounding the total rates will not always equal the sum of the in situ and invasive rates.

of total rates. Cities A and B with 4.7 and 4.25 per 1,000 have particularly high rates compared to the low rates of cities D and G with 2.26 and 1.83 respectively. The rates for the cities falling between these two groups approximate one another closely, ranging from 2.98 for City F to 2.83 for City C.

Though the rates for in situ lesions do not fall in the same order cities A and B once again have the highest rates and cities D and G the lowest with city F, which outranks them in total rate, having a lower in situ rate than either city E or C. Invasive rates are greatest in the three cities with the highest total rates. Cities E, C, D, have rates closely resembling one another but in inverse order to their total rates. The cities with the highest total rates for cancer of the cervix, cities A and B, have the highest rate of both in situ and invasive lesions.

In comparing the in situ and invasive rates it is noted that cities A, B, and E show higher in situ than invasive. For cities C and G the two rates are almost equal. Cities F and D, on the contrary, have higher invasive than in situ rates.

Conclusion

This study was undertaken with the primary purpose of determining the relationship between the incidence of in situ and invasive cervical cancer and socioeconomic status in Connecticut cities. The results indicate that the classical inverse relationship was evident for the seven metropolitan areas combined. The rate of cancer of the cervix was greater in low socioeconomic areas.

However, the inverse relationship was not constant when the cities were studied separately. In some, the rates after rising, reached a peak and then decreased in the lowest socioeconomic areas. It is difficult to explain this reversal in the inverse trend. It would seem that rather than represent a lack of cervical cancer among the very poor it instead may be due to lack of detection. The low SRA's contain by definition persons who are poorly educated and often many who do not speak or understand English. Women in these areas sometimes have neither the means nor inclination to seek medical care. Often medical facilities are not available or the women are unaware of those that could be utilized. Though it is expected that cervical cancers would eventually be diagnosed in late stages in these women this may not be the case, death may be attributed to other causes.

The direct relationship between cervical cancer and socioeconomic status in one city, an unexpected reversal in trend, cannot be readily explained. It may be due to a homegeneity of population. A more probable explanation would be increased diagnoses of in situ lesions in upper socioeconomic women through increased cytological screening carried out by their private physicians. The strong direct relationship between socioeconomic area and in situ cervical cancer in that city would seem to indicate that this is the explanation.

Because the use of Pap screening does increase the detection of cervical cancers in the non-invasive, in situ, stage it is probable that the low in situ rates for all SRA's in several cities are reflections of less active screening of all women in those cities.

Connecticut is a small state. The environmental factors and population make up of the seven metropolitan areas differ very little. It is therefore probable that the differences in invasive cancer rates between cities may also represent decreased detection of such lesions.

The variations in rates of cervical cancer found between seven metropolitan areas in Connecticut and variations in patterns within the cities were unexpected. Further study is being carried out in an effort to investigate the differences more fully. The findings will be reported at a later date.

A comprehensive report of this portion of the study from the demographic standpoint is to be presented as a Bulletin of the Agriculture Experiment Station of the University of Connecticut.

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Drug Induced Systemic Lupus Erythematosus Due To Quinidine

Frederic P. Anderson, M.D. and Gary R. Wanerka, M.D.

Introduction

The onset of a syndrome similar to systemic lupus erythematosus (SLE) has been reported in association with a number of drugs. Recently described was the case[1] of a woman who developed clinical findings and biopsy changes compatible with SLE following 18 months of quinidine therapy. Although repeated LE cell preparations were negative, this is the first recorded case of SLE attributed to quinidine. The purpose of this communication is to report another case of SLE apparently induced by quinidine in which the LE cell preparation was strongly positive.

Case Report

G. B., YNHH #44-73-54. A five year old girl was first seen at the Yale-New Haven Hospital in January, 1959, for an initial attack of paroxysmal atrial tachycardia (PAT). A chest X-ray showed pulmonary vascular congestion and pleural effusion which cleared rapidly after digitalis was administered and a normal sinus rhythm was restored. In the subsequent two years, the child was hospitalized on ten occasions for control of her arrhythmia. During this time, thirteen blood counts including smears for platelets and eight urinalyses were normal.

In February, 1961, quinidine gluconate (600 mg. every 12 hours) was started and resulted in good control. Over the next few months, dosage was reduced to 200 mg. twice daily.

She remained well until December, 1963 when an episode of severe epistaxis occurred. Over the next five months, recurrent episodes of mild epistaxis were noted. In May, 1964, when the child was 11 years old, she was admitted to the hospital because of intractable epistaxis. Laboratory findings from that admission are shown in the Table. Despite thrombocytopenia and prolonged prothrombin time, epistaxis ceased spontaneously and did not recur. Quinidine was discontinued on the fifth hospital day. Several episodes of PAT ensued which responded to reserpine administration.

Slight leukopenia was present on several occasions and the erythrocyte sedimentation rate was elevated throughout hospitalization; abnormal liver function tests were also noted. On hospital day 17, the child was found to have a low grade fever, pericardial friction rub, and slightly enlarged liver. LE cell preparations were found to be strongly positive at this time. A 4+ direct Coombs test was found, but there was no anemia and no evidence of hemolysis. The electrocardiogram and chest X-ray were normal as were liver function tests. The thrombocytopenia was improving. A fleeting generalized maculopapular rash was noted several days later. The pericardial friction rub disappeared after four days, but low grade fever persisted until discharge on the 23rd hospital day. She was asymptomatic at that time.

Urine examinations including a 12 hour Addis count were normal during hospitalization. The blood urea nitrogen (BUN) and creatinine were normal. A blood sample was sent to Dr. Irving Schulman at the University of Illinois who determined that the patient's serum failed to inhibit clot retraction or prothrombin consumption when added to normal platelet containing blood plasma. He concluded that the thrombocytopenia was not directly attributable to quinidine sensitivity. This test is qualitative, and standards are not well established.[2]

In July, 1964, 54 days after discontinuing quinidine, the LE preparation was negative. However, serum antinuclear factor was strongly positive in January and April, 1969. Examination of her urine revealed a 2+ protein on two occasions in January, 1965. Four Addis counts have been normal since this finding, and a 24 hour specimen contained less than 100 mg. of protein. In May, 1969, the the serum complement (C_3) was normal at 165mg% and the BUN, creatinine, and liver function tests were normal. She has had no further hematologic abnormalities. Since May, 1964, her PAT has been well controlled on digoxin and reserpine, and she has had no further clinical evidence of systemic disease.

TABLE

LABORATORY FINDINGS

		Hospital Day		
	Admission	*6-7*	*16-17*	*20*
WBC (per mm³)	5550	4850	5150	4650
Platelets (per mm³)	22,550	14,000	100,000	120,000
ERS (mm/hour)	40	35	64	39
Prothrombin time (percent of normal)	40	87	64	28
SGOT (normal is 15 to 35)	56		15	
Cephalin flocculation	4+		2+	
Thymol tubidity	11		5.7	
LE preparation			4+	
Direct Coombs			4+	

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Discussion

It has been suggested from studies done on predominantly adult populations that between 3% and 12% of cases of SLE are drug induced.[3] Review of the literature, however, reveals only a single case reported in which the development of symptoms of SLE was attributed to quinidine.[1]

This drug has been reported to cause various toxic manifestations[4] including dose-related cinchonism and a variety of idiosyncratic reactions with neurological symptoms, fever, skin rash, angioedema, thrombocytopenia,[5] and hemolyticanemia,[6] and granulocytopenia.[7]

Shulman has studied quinidine induced thrombocytopenia as a model system of induced cytotoxicity demonstrating the steps of antigen-antibody reactions, absorption of the complex to platelets, and subsequent complement utilization and cell destruction. He points out that mechanisms similar to this are seen in auto-immune disorders, the only difference perhaps being in the latter's absence of a recognized foreign antigen. This capacity of quinidine to become involved in an antigen-antibody reaction may relate to its role in the genesis of the SLE syndrome in this girl.

Although the present patient presented with thrombocytopenia, she had evidence of multiple system involvement with fever, skin rash (thought at the time, without confirmation, to be due to rubella), hepatic involvement, pericardial friction rub, positive direct Coombs test, thrombocytopenia, and a positive LE cell preparation. Subsequent study indicated that the thrombocytopenia probably was not due directly to quinidine sensitivity but was one manifestation of a more protean disorder. The medication is implicated as the cause of the clinical findings because of regression of symptoms after discontinuation of quinidine with reversion of the LE cell preparation to negative. Her subsequent asymptomatic course in the face of a persistently positive ANF is compatible with that seen in drug induced SLE.[9] Quinidine rechallenge has not been attempted.

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Patient Requests for Controlled Drugs

Franklin M. Foote, M.D.

In a variety of ways it appears that those persons seeking prescription and controlled drugs are cajoling physicians into prescribing or dispensing such drugs on questionable indications.

In some cases, physicians specializing in treatment of obesity cases appear to be relying chiefly on the dispensing of amphetamine type drugs to curb the appetite. Some such physicians seem to have built up a substantial practice which has appeared to give little consideration to other methods of obesity control such as exercise and diet. Despite recommendations of the manufacturers and of the American Medical Association that amphetamines be used for weight control for periods not in excess of 6 to 10 weeks, some physicians have dispensed them to patients once a month over a period of several years with the patient gaining 20 or 30 lbs. more than when he or

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DR. FRANKLIN M. FOOTE, Commissioner of Health, State of Connecticut, 79 Elm Street, Hartford, Conn.

she first came under the care of the physician. In other cases, amphetamine type drugs have been dispensed to young men in their teens and early 20's who were of average weight for their height and age, who report to our investigators having had a cursory medical history taken and superficial medical examination. Some such physicians have been presented in court for violation of the statutes or to the Connecticut Medical Examining Board.

In other cases, physicians appear to be prescribing or dispensing tranquilizers, sedatives and amphetamines to more mature individuals in considerable quantities and over long periods of time without psychiatric evaluation. In some of these instances the patient sees two physicians simultaneously without either one knowing that the other also is prescribing or dispensing the medications requested.

Even more of a problem is created when such patients telephone physicians who may or may not have seen the patient years before and request a small supply of controlled drugs on the basis of a telephone prescription to a drugstore. Such individuals are imaginative and exceedingly clever in telling a story to a busy physician on the telephone which results in his calling the pharmacist to authorize the dispensing of 20 or 30 doses of the drug requested.

From time to time the state department of health receives telephone calls and letters from the families of some of these unfortunate individuals. Below for example is the kind of letter we not infrequently receive which we felt on this occasion should be shared with physicians throughout the state:

> 'I write this letter as a plea for help in a situation which may soon very well claim the life of my wife. I refer to the promiscuous and irresponsible issue of prescriptions for barbiturates by doctors on the basis of a telephone request without ever seeing the individual or making the slightest attempt to check their medical history.
>
> "My wife has a long history of addiction to alcohol and barbiturates. In some years she has been institutionalized as much as 270 out of 360 days. More recently she has found it as easy to obtain bariturates as she had alcohol in the past. By merely calling a doctor at random from the phone book, presenting a logical story of a casual need for these drugs, she has been successful in maintaining an almost inexhaustable supply. I enclose some of the prescription labels I have collected over the past few months.
>
> "Having been hospitalized already for 80 days this year, my wife is now at .... hospital for what appears to be an extended stay. Although restricting or eliminating this source of supply will be of little help to her, I can't help but think that some program that will make the medical profession aware of the incredible havoc they cause by this indiscriminate dispensing of these most harmful drugs, may certainly help others."

It is urged that in view of the increased tendency for certain persons to demand amphetamines, tranquilizers and barbiturates, physicians generally develop a strong resistance to these requests and where there appears to be an emotional or neurotic problem which the physician cannot manage without excessive use of these medications, that he consider referral to a psychiatrist or a mental health clinic as a means of avoiding being persuaded to participate in the prescription of undue quantities or over undue periods of time.

If a man is able to lead a purposeful, challenging life and is doing so remains flexible enough to change when change is needed, resourceful enough to admit mistakes when they are made and interested enough to continue to study and stay abreast of things, then he would enjoy a happy professional career.—Dr. Waldo E. Martin.

Connecticut Medicine

Editorials

Connecticut Surgeons and Cooperative Clinical Research

Cooperative clinical studies originating from a group of institutions, whether prospective or restrospective in plan, have almost always been carried out by university-affiliated physicians. One very important purveyor of patient care—the community physician not directly associated with a medical center—has infrequently been involved with such studies, perhaps largely due to lack of an administrative base. In Connecticut we are fortunate to have an organization of surgeons with some members on the faculty of Yale University or the University of Connecticut but most community-based and all certified by the American Board of Surgery. This group, The Connecticut Society of American Board Surgeons, was founded in 1948, "for the improvement of surgery in Connecticut" to quote its bylaws. To the present time this organization has been the only spokesman for the general surgeon in the State and it has assisted when official or unofficial bodies have sought the view of the general surgeon in Connecticut and has long represented this specialty in the Connecticut State Medical Society which lacks a general surgical section.

A few years ago some organizational soul-searching disclosed that the CSABS might become an important sponsor of cooperative research undertakings encompassing the State, since its membership served an excellent population-based sample of patients, a desirable study group but one which is seldom attainable. The Executive Committee of the Society discussed possibilities and after consultation with its membership launched a study of the surgical management of massive upper gastrointestinal hemorrhage in Connecticut, the first State-wide study of this type. Twenty-eight hospitals, representing 90 per cent of the acute medical-surgical beds in Connecticut, and numerous surgeons contributed data. A tremendous amount of time and effort was required to gather and collate the data and the results of a one-year experience has recently been published in *The American Journal of Surgery** under the authorshop of the CSABS. No startling new concepts of therapy were uncovered but a clear picture of management of a common medical emergency in our State does emerge.

The success of this project challenged investigation in other areas of medical care and the CSABS is currently conducting a study of acute abdominal trauma. This new study is prospective and the cooperation of surgeons has been outstanding. The active participation of the CSABS membership serves to demonstrate conslusively that significant and meaningful clinical research can be conducted outside the formal educational environment by community-based physicians.—I.S.G.

A Crusade Against Arteriosclerosis

Several years ago the Regional Medical Programs were set up and funded to control heart disease, cancer and stroke. Many millions have been spent on these efforts in the various states. Apparently not satisfied with the progress made a panel of consultants a year ago persuaded Congress and the President to launch a separate crusade against cancer. It is expected that in the next three years 1.6 billion will be spent in active pursuit of this goal.

Now a much larger national program aimed at improving prevention and treatment of arteriosclerosis and at stimulating research into its causes has been recommended by a task force set up under the auspices of the National Heart and Lung Institute. The report is aimed at launching a crusade against cardiovascular disease in much the same way as the report of a panel of consultants a year ago launched a crusade against cancer. The forthcoming debate about the merits of implementing the report recommendations will be an interesting lesson in the way Congress and the Administration will set about dealing with large but scientifically and emotional strong claims from different sectors of biomedical research.

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* Immediate Results of Emergency Operation for Massive Upper Gastrointestinal Hemorrhage. American Journal of Surgery 122: 387, (September).

The report was prepared by a 15 member task force under the chairmanship of Dr. Elliot Newman of Vanderbilt University and later by Oglesby Paul of Northwestern University.[1] It calls for a program that will cost 120 million in the first year and 175 million in the second year above the funding of 104 million for research and treatment of arteriosclerosis. The basis for this request is that arteriosclerosis is the number one killer in the United States and that there already exists a strong base of knowledge which would allow programs aimed at preventing the onset of the disease to have a significant effect on mortality in this country.

Throughout the Congressional debate on cancer, it was repeatedly emphasized that the disease affects about one person in four. This argument is considerably strengthened when it is applied to arteriosclerosis for the task force points out that arteriosclerosis is directly or indirectly responsible for nearly half of all deaths in the United States each year. The disease is most prevalent among individuals with a variety of "risk" factors prominent among which are three specific ones, high levels of blood lipids, high blood pressure and cigarette smoking.

The task force, therefore, sees the chief aim of any Federal program as an intensive effort aimed at public education linked with an expanded research effort aimed at discovering more precisely the levels between various factors and onset of the disease.

That arteriosclerosis is caused in large measure by extraneous factors such as personal habits and environmental factors can be inferred from the huge discrepancies in the prevalance of the disease among different countries. The U.S. ranks second in the international rating and arteriosclerosis occurs ten times more frequently here than in Japan. This discrepancy would lead us to infer that if we knew why this difference existed and could alter the conditions in this country to those in Japan the disease might be cut by 90 percent.

Among the chief recommendations of the task force are the following. Several centers devoted to the study and treatment of all factors of arteriosclerosis should be established in existing hospitals and universities. At present, the effort is fragmented into small programs at many universities and hospitals. Excellent as these programs are they do not encompass a multi-disciplinary attack on the disease. Called National Centers for the Prevention of Arteriosclerosis, the centers would be focal points for the detection, prevention, arrest and reversal of the disease and they might be modeled on other mission oriented governmental research centers such as Lawrence Livermore Laboratory or the Oak Ridge National Laboratory.

Smaller cardiovascular disease prevention units should be established within the framework of existing health care. They will be charged with the task of screening persons to detect those most at risk and would also serve as a means of collecting together information on the prevalence of the disease and its dependence on different factors many of which we already know from the superior work at Framingham. (see front cover)

The task force also suggests that an Office of Health Education should be established in the National Heart and Lung Institute to serve as a clearing house for information on arteriosclerosis. The office would be partly responsible for public education about the risks associated with, for example, cigarette smoking and the advisability of having regular checks of blood pressure.

As far as research is concerned the task force suggests that efforts aimed at primary prevention of arteriosclerosis are presently not based on adequate information and that a vigorous effort of basic and applied research will provide the knowledge required for efficient prevention programs. The research would be carried on primarily in the suggested National Centers for the Prevention of Arteriosclerosis. The report suggests large scale programs of applied research to test the so-called "risk" factor hypothesis.

The chief problem with such trials, however, is that they would involve large numbers of patients to be studied over long periods of time. However, with the increase in the numbers of patients under observation in the National Centers, several important questions concerning the causal relationship between factors such as high blood pressure and high blood lipids could be resolved.

Finally the task force recommends that the National Heart and Lung Institute should engage in an expanded program of basic research to elucidate, for example, factors which govern the levels of lipids in the blood and the mechanism whereby genetics, hypertension, cigarette smoking and other risk factors affect the formation of arteriosclerotic plaques on the arterial walls.

One major difference between this report and last year's report of the panel of consultants on cancer, is that this task force makes no recommendation for taking arteriosclerosis research outside of NIH whereas the one on cancer got tangled up on its recommendation to set up a separate institute for the purpose.—L.H.N.

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Multiphasic Screening Supplements Physical Examination

Bates[1] has raised the question of whether multiphasic screening alone is sufficient to keep the "well" and "well but worried" patient from inundating and overloading the busy physician in his practice. Accordingly, he designed studies to test whether screening can identify most if not all of the problems that would be found by the physician. He studied 47 persons ranging from 16-61 years of age that were examined independently by a clinical examination done for routine preemployment screening and by a full multiphasic screening evaluation which included a c.b.c., VDRL, 19 blood chemical measurements, visual acuity, visual fields, tonometry if over age 35, audiometry, urinalysis, screening urine culture, height, weight, blood pressure, spirometry, miniature chest X-ray, ECG and the Cornell Medical Index Health Questionnaire.

The clinical examination consisted of an initial screening interview conducted by a nurse focusing on past medical treatment and current health, physician's general physical examination (excluding pelvic and rectal) with concurrent interview and diagnostic studies of which urinalysis and chest X-ray were routine. Apparent problems were identified independently both from the clinical evaluations and from review of the clinical reports. The problem lists for each patient were tabulated according to the system suggested by Weed.[2] The clinically derived lists were then compared against those based on the screening reports. In addition, for each listed problem a judgment was made as to whether it permitted employment without restriction, indicated employment only with restriction or required further evaluation before employment.

A comparison of the problem lists derived from the two methods showed little overlap in the conditions identified. Of the total of 180 problems suggested by the two methods only 30 cases of the 15 conditions were suggested by both. Forty-seven cases of 31 conditions were found on clinical evaluation alone ranging from systolic murmur all the way throughout the body. The problems found on screening alone accounted for 57 percent of the apparent problems suggested, apparent problems identified only on multiphasic screening also included clinical conditions most of which were based on the "health questionnaire."

Some of the "apparent problems" may be relatively minor. Six cases of 5 conditions were found on clinical examination such as back problems, peripheral vascular disease, diabetic neuropathy and diabetic retinopathy. Eighteen cases of 14 conditions were found only on screening. Because the number of problems identified in common by both methods was surprisingly low, a second study was done to test the possibility that the results might be peculiarly limited to the preemployment evaluation of job seekers. From the medical clinic of a university hospital 12 patients were identified who had had clinical evaluation followed by multiphasic screening problems. Problem lists from each source were completed and compared as before. The results were similar.

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Of 115 problems, 17 percent were identified both by clinical evaluation and screening, 21 percent by clinical evaluation alone and 62 percent by screening alone. Calculations from both studies show that screening alone identified from 38-45 percent of the problems recorded in the clinical evaluation. Chart reviews of the clinical material identified from 23 percent of the apparent problems suggested by screening.

The problem now arises how well two independent physician raters will agree on the problems identified (inter-observer reliability) and how well any one rater will agree with an earlier rating he made (intra-observer reliability). Bates in a third study on 18 reports the physician involved in the previous study and a second internist compared their problem lists against each others and against their problem lists completed seven months earlier. Inter and intra observers agreement clustered between 56 and 66 percent. These inconsistencies in observation occurred despite the fact that all laboratory values outside the normal ranges were automatically starred. Comparable variations have been found in physical examinations[7] and in the interpretation of the ECG[4] and chest films[5] in medical[6] and psychiatric diagrams.

Present evidence supports the conclusion that multiphasic screening and clinical evaluation are significantly different in the kinds of conditions they identify. If screening is used to replace the physician's examination many apparent problems will be missed that are primarily ascertained by physical inspections, examinations and interactions between physician and patient.

Likewise, clinical evaluation fails to identify a subset of problems potentially detectable by screening. This group constitutes a considerably larger amount of the total problems, slightly more than half are derived from laboratory studies. Thus rather than being a substitute, the two systems evaluation supplement each other. —L.H.N.

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Relation Of Neoplasia To Dietary Practices

The association between diet and the development or prevention of cancer has from the earliest times proved to be a fertile field for a wide range of speculation from food faddist to epidemiologists. However, an objective approach also permits views about diet composition and practices in food preparation as factors which may influence tumor development. Gastrointestinal neoplasia have been of special interest to the epidemiologist since the incidence of malignancy in both the upper and lower areas of the alimentary tract is often high and survival rates are low.[1]

An association has been noted between Plummer-Vinson syndrome believed to be secondary to iron and vitamin deficiency and cancer of the hypopharynx in Swedish women. Esophageal cancer has an extremely high incidence especially among males in certain areas of Europe, Asia, East and South Africa, but is practically unknown in West Africa. The high incidence tended to be found in heavier smokers and drinkers and who consumed less milk, eggs and leafy vegetables than did the controls.[2]

Gastric cancer shows large demographic differences. Japan, Chile, Austria, Finland and Iceland have rates predominantly in males 4 or more times than those of U.S. whites. In Iceland the high incidence is thought to be related to the large intake of smoked food perhaps in association with a reduced vitamin C intake. The process of smoking food is believed to produce carcinogenesis. It is postulated that in Japan the high incidence of gastric cancer is due to the preference for talc dusted rice because the talc may contain asbestos.

Death rates from cancer of the colon have a strong negative correlation with those of gastric cancer, the one being common where the other is rare. In this country and England, colon cancer is second only to lung cancer in numbers of deaths—12-14 percent of all deaths from malignancy. Studies in New Yorkers has led to the suggestion that cancer of the colon is corre-

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lated with a high fat intake. In Japan where colonic cancer is uncommon, fat intake is about 12 percent of the total calories and mostly of the unsaturated type compared to 40-44 percent figure in this country.

Japanese immigrants, however, and especially their children born in the U.S. have a much higher incidence of colon cancer than those of Japan. This same trend has been noted also for Puerto Ricans after they come to this country. Japanese with colon cancer have a higher socioeconomic status and tend to eat diets with more fat calories. In Czechs the rate of gastric cancer is twice and for intestinal cancer half of ours. Their diet is appreciably lower in animal derived protein and fat and in vitamins.

Various authors have pointed out that populations in areas with a high incidence of colonic cancer tend to consume diets relatively high in refined foods and low in fiber foods whereas those where the incidence is low, subsist largely on vegetarian diets with relatively little animal products. The refined food diets result in relatively small stool volumes and prolonged intestinal transit time in the colon whereas large stools and more rapid transit is associated with high cellulose diets.[3]

There are also differences in the bacterial flora associated with the different types of diets. Consumers of the "western type" diets were found to have higher concentrations of fecal steroids which tended to be more degraded than did those of vegetarian diets. Perhaps bile metabolites may be carcinogenic. Obviously, if carcinogens are produced by bacterial action then delayed transit time would permit increased bacteria formation as well as prolonged epithelial exposure.

Primary liver carcinoma is a major problem in the males of certain population groups, in Africa, South China, Hawaii and Rumania. In sub-Saharal Africa this is the most common of all forms of cancer. In Bantus and in Mozambique it accounts for 2/3 of all tumors in men with a rate of 500 times that observed in the U.S. This difference in liver cancer is primarily confined to tumors of hepatocytes. One suggestion is that the high frequency in Africa and Asia is due to a higher proportion of cirrhotic livers developing neoplastic changes and that a similar trend is occurring elsewhere.[4]

The effect of fat intake upon cancer was studied over an 8 year period in elderly men in an institution in California where the patients subsisted either on conventional diets or one high in polyunsaturated fat and low in saturated fat and cholesterol.[5] They found a decreased incidence of fatal atherosclerotic events in the group on high unsaturated low saturated fat diets, but an increase in fatal carcinomas of various types. The explanation for this finding is unknown but a similar finding on the incidence of tumors and mortality was found in rats and mice when unsaturated fat was increased in their diets.[5]

A definite positive correlation was found between incidence of cancer and overweight. It appears that cancer of the alimentary tract, liver, gallbladder and also of the genitourinary tract were positively associated with weight.[6] A statistically significant association with weight has also been noticed between obesity and colonic cancer in males. There is also good evidence that cancer of the uterus occurs more frequently in overweight women. Obesity, of course, is also associated with hypertension, diabetes and irregular menstrual bleeding. Thus far there are no data on the obvious question of the possible beneficial effect of persistent weight reduction on the incidence of tumor development.—L.H.N.

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Biomedical Research And Human Health

Of all research being done in every area of our social fabric, biomedical research alone consistently improves the quality of life and the welfare of man. Towards this end, the government has appropriated 1.5 billion dollars last year compared with 4 billion for space, 2 billion for the Department of Defense. Research in space and defense have increased by 12 percent but only 2 percent in biomedical research. Considering inflation, appropriation for biomedical research is an actual decline. It might be appropri-

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ate to evaluate the costs and benefits of biomedical research versus the other forms of research in terms of the possible scientific and economic benefits. It has been estimated, in fact, that money given SST must produce detrimental effects on human health, 23,000 to 100,000 additional cases of skin cancer per year which would be caused by 800 SST's affecting the ozone layer which now filters out the ultraviolet rays.

People are asking what can be done to improve the delivery and quality of medical care. But they should also be asking what can be done to reduce the need for medical manpower by eradication of disease. For example, 30 million people in this country have some form of cardiovascular disease and disability and over one million die each year as a consequence of such illness. How many physicians would be freed for other work in poverty and rural areas if we could reduce cardiovascular disease?

If we were able to postpone the onset of cardiovascular disease for 5-10 years and this is not an unreasonable goal for the next decade provided our research momentum is maintained, the savings would be many billions. How much greater would be the G.N.P. in a given year if morbidity and premature mortality from these diseases had not intervened. The National Center for Health Statistics has estimated that for the year July 1966 to June 1967, the average annual number of disability days for cardiovascular disease was 160 million for bed disability and 452 million for restricted activity.

The polio history is an excellent example of what biomedical research can do. Formerly poliomyelitis swept across this country periodically in epidemics. There were thousands of helpless patients needing night and day care in "iron lungs". There were terrific financial burdens conferred on families of these patients, a long list waiting for beds in orthopedics wards for corrective surgery followed by weekly painful trips to the rehabilitation clinics. In 5 years before the vaccine was introduced in 1954, 30,000 cases a year were reported and 2,500 died. In the last 5 years only 60 cases were reported a year and last year none was reported. Thus, in 15 years since the introduction of the vaccine several hundred thousand people have been spared the disease and hundreds of physicians freed for other pressing medical problems. But it took over half a century to solve the problem. We should not look for miracles.

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Warnings
When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.
Drug Dependence Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with the high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.
Usage In Pregnancy The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.
Usage In Children Not recommended for use in children under 12 years of age.

Precautions
In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorectic agent and a restrictive dietary regimen.

Adverse Reactions
Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration
The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

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Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.
Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

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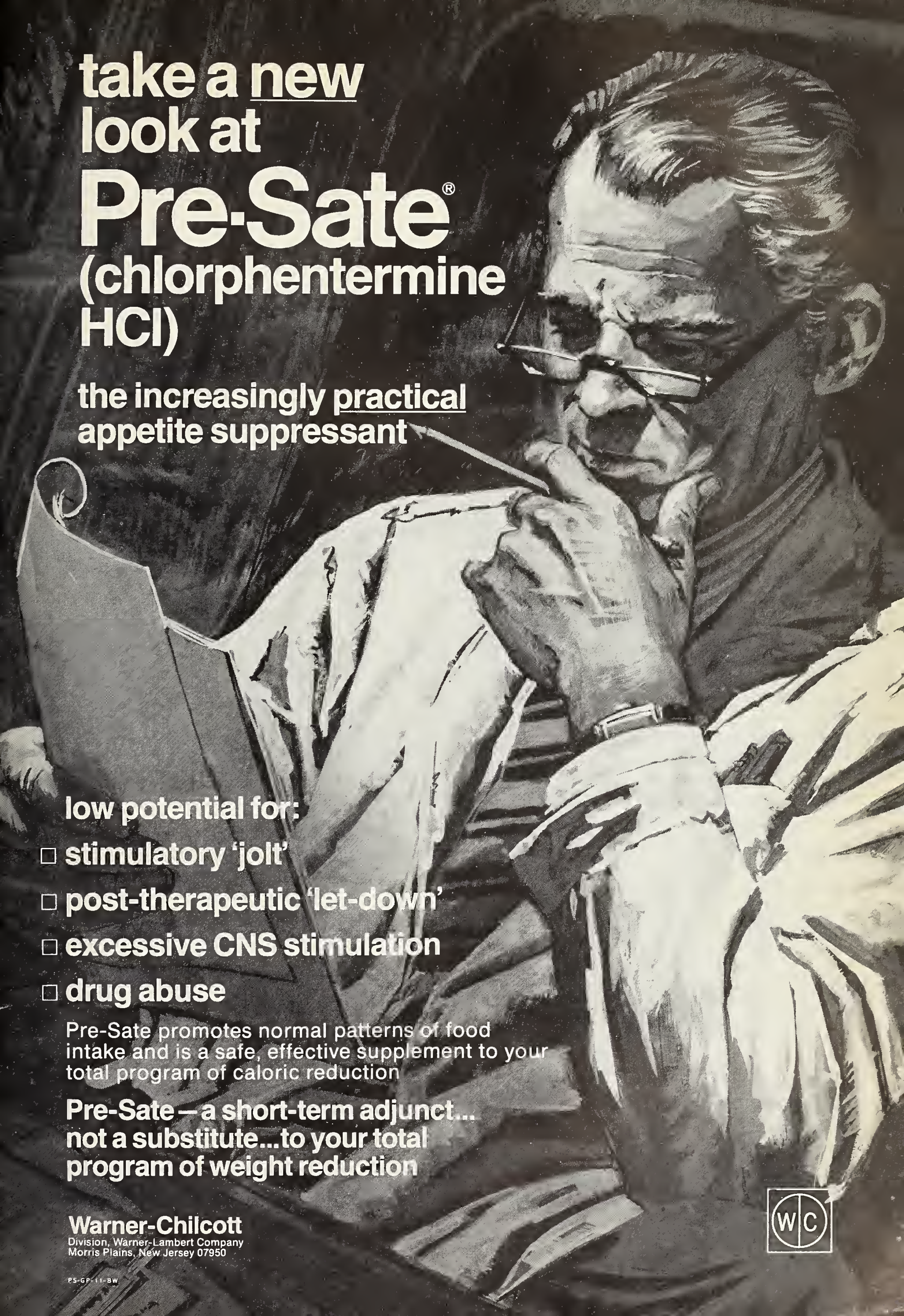

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Then there is the economic side of the problem with patient care alone amounting to many millions of dollars a year prior to the introduction of the polio vaccine. If one adds to this figure the life time earnings of those who might have had the disease and the production losses, it adds up to many billions. This is a result of a research investment of only a few million. Here is one way biology and medicine fight inflation. Actually, the polio problem is miniscule compared to that of cardiovascular disease. The direct cost per year for care of these patients is 5.1 billion and indirect cost 25.4 billion.

Thus billions are lost each year in productivity. Recently, President Nixon appointed a Commission on Productivity and stressed that everyone must do his utmost to increase productivity if inflation is to be controlled. Let us hope the Commission will be able to convince the President that the biomedical community can be powerful allies in this fight. But they cannot do so by decreasing biomedical research funds. This is dangerous. Were it not for the effects of basic biomedical research performed ten years ago, the nation's total health bill would probably have been 100 billion rather than 70.

The recent decreases in funding for the NIH research and training grants have already caused many young people who had contemplated academic careers in biomedical research to alter their career decision. The biomedical research expenditure policy has been a mild disaster in the past two years. Unless altered, it will in the next two years serve to eradicate a generation of future researchers. It will dismember the present good biomedical research establishment and will require many years to recreate them.

With more adequate support for medical education and medical research we can help to reduce the pain and grief of millions of our citizens and to improve the quality of life and the welfare of man.—L.H.N.

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Some Advances In Our Knowledge Of Homosexuality

The normal sexual behavior represents a complex interplay of psychic, neural and endocrine factors, each of which can influence the other. Traditionally, homosexual behavior has been regarded as a result of psychosocial factors operating during infancy and childhood. Homosexuality has always been an integral pattern in human sexual behavior. Socarides[1] estimates conservatively that between 2.5 million and 4 million American males are homosexual. Kinsey[2] states that 4 percent of white males are exclusively homosexual throughout their lives after the onset of adolescence and that 18 percent of the total male population have at least as much homosexual as well as heterosexual activity for a minimum of 3 years between ages 16-55.

An intact autonomic and endocrine system is of course necessary for the development of sexual drive and potency and the view prevails that it can be strongly influenced by emotional and psychologic factors. The question has remained in the minds of investigators whether homosexuality can be explained on grounds of hormonal dysfunction. Most studies in the past have used urinary 17 ketosteroids as the index of androgenicity. But this line of investigation proved inadequate because of the potency of testosterone and the small amount it contributes to urinary ketosteroids.

Last year Margolese[3] described an abnormality of testosterone metabolism in homosexuals and now Kolodny et al[4] have reported at length on serum testosterone levels and sperm counts in a group of male homosexuals with an impressive correlation between the degree of defect and the rated degree of homosexuality. These studies were made possible by an extraordinary increase in specificity and sensitivity of the new method of hormone assay.

Kolodny studies 30 male homosexuals, rated according to degree of homosexuality, for plasma testosterone levels, semen counts, and buccal smears. They found that the homosexual averaged less than half plasma testosterone by comparison with normal heterosexuals of the same age group. The homosexuals also showed reduced semen counts indicating impaired spermatogenesis. These homosexuals had no evidence of overt sexual dysfunction or lowered levels of libido although the general impression persists that men with subnormal testosterone levels tend to show impaired libido as well as erectile dysfunction.

If data like that of Kolodny can be confirmed by other workers, it will open a wealth of possible speculation and research as suggested by Federman.[5] Since testosterone is known to stimulate libido in both sexes why should a lower level of it lead to a selective change in the vector of male sexual desire? Is the effect directly on object choice or is it an indirect consequence of a change in self-image produced by lower testosterone levels? Are the depressed plasma testosterone levels a secondary result of a primary homosexual psychosocial orientation with depressive reaction through the hypothalamus from higher cortical centers?[5]

Obviously, there must be definitive endocrine evaluation before a secure position can be established. At present, we can only speculate. But there are currently advances in two areas that should accelerate our clarification of the problem. One is the biochemical advance in hormonal assay which has deepened our knowledge of hormonal function and the other is the broadened interest and candor in the study of human sexuality.

The interweaving of these themes should soon enable physicians to understand better and to help many patients who suffer from disordered sexual behavior.—L.H.N.

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Tumor Immunology: Tumor Specific Antigens In Hodgkin's Disease

At the beginning of this century claims were raised that tumors are antigenically different from normal tissues. Only sixteen years ago, however, did valid evidence appear for the existence of tumor-associated antigens. Most of such evidence since has come from work on animal tumors. Today it is a more or less accepted fact that the majority of tumors originating in experimental animals have antigens that are absent at least in corresponding amounts from normal tissue. Order[1] calls attention to the fact that many human tumors have been found to have tumor associated antigens also including colonic cancer, neuroblastoma, melanoma, soft-tissue and osteogenic sarcomas, ovarian carcinoma, bladder cancer and Burkitt's lymphoma.

Order, et al, present evidence for the existence of a common antigen in neoplastic cells from a human tumor, Hodgkin's disease. They used immunoflourescence in combination with heteroimmune serums. The unique circumstance in Hodgkin's disease of removing the spleen for staging purposes (well described by Nuland in a previous issue of this Journal) made it possible in their studies to use both normal and abnormal tissue from the same organ. This allowed for absorption of histocompatibility antigen with the grossly normal splenic tissue from the same patient. Their preliminary results indicate that Hodgkin's disease as with many other human cancers, is associated with an antigen.

It remains to be determined whether such antigenicity is unique for Hodgkin's disease and found in all forms of the disease or in all anatomic locations. Common antigens may indicate expression of embryonic antigens[2] or may indi-

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cate viral etiology and both possibilities need to be investigated. It is not yet known whether such antigens are located only on the surface of the tumor cells or in the reactive stroma or both.

One may argue that the paper by Order, et al, is quite preliminary with only those patients studied or that the reactions detected may not have been directed against a tumor-associated antigen but against normal tissue-specific antigens present in a higher dose on the neoplastic cells. However, the evidence is suggestive of a new antigen in Hodgkin's disease by indicating that the antigens were obtained from sections of tumor tissue taken directly from these and not previously cultivated in vitro.

Tumor immunology is one of the branches of cancer research to which our hopes go for an ultimate prevention and cure of at least certain tumors. The interesting evidence for new antigens in human cancers and the demonstrations of immunologic reactions in many tumor patients against their own neoplasms however, is still very far from a solution of the cancer problem. The door may only be slightly ajar rather than wide open for the immunologic prevention and cure of human tumors. Even in experimental animal systems where there is overwhelming evidence for a specific tumor immunity, it has not been possible except in very special cases[3] to prevent or cure primary tumors immunologically.

This by no means implies that immunology has nothing to offer for the ultimate realization of those goals. It just tells us that we need to know better the immunologic mechanisms that can sometimes kill a transplanted tumor in vivo but often fail or are blocked[4] thus permitting an antigenic tumor to grow in vivo. Perhaps the answer will come when we develop better animal models for immunologic prevention and care of tumors. The increasing evidence for the existence of human tumor-antigen acts as a strong impetus for such work.

It is realistic to hope at least that better understanding of immunologic reactions against tumor antigens will promote clinically useful ways of ultimately improving the ability of patients with cancer to destroy their own tumor cells.—L.H.N.

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Science Tools: A Method Of Estimating Penile Blood Pressure

It appears that normal penile systolic pressure as measured by a spectroscopic method is equal to or greater than the calculated brachial mean blood pressure.[1] A proximal event in the process of erection is a dilatation of the penile arteries resulting in a marked increase in blood flow to fill and distend the sinuses of the erectile tissue.[2] If the penile arteries are constricted it results in an abatement of erection. If in a patient a penile pressure definitely lower than normal is found, he could be impotent. Such a situation could be expected in obstruction to blood flow in the main vessels supplying the penis. On this basis obstruction to blood flow has been identified as a cause of impotence. Such patients of course could have advanced interference in blood flow as occurs in aortic obstruction at the bifurcation. But the arterial disease can occur in the penis even when there is little other evidence of peripheral vascular disease.

Generally it is believed that impotence is of psychogenic origin in the great majority of patients. However, Johnson[3] recognized that there are forms of impotence for which no physical or psychological explanation can be offered although reactive psychic symptoms can develop in the patient secondarily. Arterial obstruction in vessels supplying the penis is not given prominence as a possible cause of impotence. Johnson says that "impotence may rarely be due to the blood supply to the penis in thromboobliteration of the bifurcation of the aorta ("Leriche Syndrome"). Others discuss the etiology of impotence without including arterial obstruction as a cause at all.

It is not well enough appreciated that arterial obstruction in the vessels supplying the penis may cause impotence in the absence of Leriche Syndrome or even in the absence of any gross obstruction to blood flow in the main vessels supplying the lower limbs. Possibly this is because those concerned with peripheral vascular disease have paid too little attention to impotence as a symptom, especially in older men but perhaps even more so because a simple method of assessing the possibility has not been suggested previously.

Gaskell studied the penile blood pressure by means of a spectroscopic method with a cuff around the shaft of the penis. He tested it in 61 patients, 14 normal young men, 17 potent patients ranging in age from 50-87, one potent diabetic patient, 22 impotent non-diabetic patients ranging in age from 39-74 and 8 impotent diabetic patients age 44-74. All impotent patients showed a striking reduction in arterial pressure in the pudendal arteries. By this means he identified one factor in impotence namely arteriosclerotic obstruction to blood flow in the penis.

In Gaskell's group most came for treatment for peripheral vascular disease and they had penile as well as peripheral blood pressures taken and were also asked about penile erection. He found that the calculated brachial mean blood pressure appears to provide a convenient fairly sensitive indicator of the minimum normal penile systolic pressure. With the measurement it is possible to identify most patients whose impotence is caused by arterial obstruction even in the absence of other evidence of gross arterial disease. Previously such patients were grouped with those whose impotence is considered psychogenic.

No large unselected series of patients with impotence has been tested in this way but clearly this now should be done and perhaps every patient with this symptom should be so tested. Whether such patients might improve with vasodilator drugs has not been reported in the literature but one prominent urologist[4] has been treating such patients in this way for a considerable period of time. Most of the patients in Gaskell's series had evidence of obstruction of blood flow in vessels supplying the penis even though they had no Leriche Syndrome and even a few with no gross evidence of peripheral vascular disease.

It is reported that impotence is a common occurrence in patients with diabetes.[5,6] Rubin and Babbott thought that neurogenic changes in the erection mechanism may be responsible but Simpson recognized that endarteritis affecting the vascular mechanism of erection may be another organic cause of impotence in these patients. Some proposed reduced testosterone levels as a cause of impotence in diabetes while others disagree.

Gaskell's study shows that obstruction to blood flow in vessels supplying the penis must be considered as a possible cause of impotence not only in diabetic patients but also in all cases of peripheral vascular disease and even others without gross vascular disease. The technology required to perform the test is relatively simple. —L.H.N.

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Cancer Of The Colon And Rectum

Cancer of the colon and rectum is the most common visceral cancer in man. In 1971 it will kill approximately 45,000 persons, roughly an equal number of men and women. Only cancer of the lungs will kill more men. Only cancer of the breast kills more women. Fortunately, up to 80 percent of patients who develop colon cancer can be cured but only if it is discovered early. To discover colonic cancer early, we must be on the alert for six clues from the history that suggest its presence and then perform the necessary investigations to confirm it.

One clue is abdominal pain which is the most common symptom of colon cancer, but only a late one in rectal cancer. The pain is referred to as "gas", "indigestion", "dyspepsia" or abdominal discomfort. Especially should cancer be suspected if these symptoms occur repeatedly. Left colon lesions tend to be annular and constricting and to produce organic obstruction and abdominal cramps. Right colon cancer tend to be bulky, seldom produce cramps. Instead, they produce a vague indefinite kind of pain simulating gall bladder or peptic ulcer disease.

Another set of symptoms is weakness, fatigue and anemia. In the absence of an obvious cause for persistent anemia, cancer of the colon, especially the right, should be thought of. Altered symptom is rectal bleeding which is common and highly significant. Even in a patient with a known history of hemorrhoids, rectal bleeding should not be dismissed but fully investigated.

Increasing constipation requiring increasing use of laxatives sometimes points to cancer. Any recent increase in the use of laxatives even in a person with a long standing history of constipation should raise our suspicion of a partially obstructing lesion of the colon. So also should any change in bowel habits such as constipation alternating with diarrhea.

Tumors of the lower rectum often give a person a sense of incomplete evacuation. An intrinsic mass which cannot be evacuated produces this annoying symptom. Such a patient requires a complete physical examination including a digital rectal examination, a procto-symoidoscopy and a barium enema with air contrast. Naturally, any patient suspected of having colon cancer should routinely be tested for blood in the stools. Such testing may also be useful in screening patients who do not have colon symptoms.

The commercially available guaiac impregnate slide make such testing simple and essentially acceptable. There are other tests used but unfortunately patients on a regular meat containing diet without open lesions may yield faintly positive reactions in almost half of their specimens, and patients on a bland diet may even reverse a positive guaiac reaction. Accordingly, to improve reliability, stools should be tested for occult blood after a meat free high residue diet. The patient should be on such a diet at least 24 hours before the specimen is collected and should remain on this diet until all the specimens are collected. Since blood may appear in the stool only intermittently, at least three consecutive stools need to be tested before accepting a negative result.

So far, explorative cytology studies of the stool have been of little practical value in detecting early cancer of the rectum and colon. However, the search is still on for a reliable early screening method.

For years investigators have unsuccessfully sought a blood test for cancer. A recent series of experiments has exciting potential for screening for colon cancer. Two Canadian investigators, Dr. S. Freedman and Phillip Gold, have shown that all human colon cancers contain an identical tumor specific antigen. This antigen called carcino-embryonic antigen or CEA, disappears from the blood of those successfully treated for cancer but not from those in whom the cancer has spread. CEA is found in cancers of the colon and also in the human embryo and fetus up to six months of gestation. There is a new radio-immuno-assay test which can detect CEA in as little as one billionth part per m.l. of serum. Further studies are now being conducted in the U.S. and Canada to determine the accuracy and reliability of this test.—L.H.N.

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Smokers' Wrinkles

Skin wrinkling is of substantial concern to many people. Traditionally it is related to wind and sun exposure, the aging process, massive weight reduction and perhaps some as yet unknown constitutional factors. Recently Daniell as had Ippen and Ippen before them noted that wrinkled skin was much more obvious in habitual smokers. He studied a total of 515 men and 589 women with regard to factors related above and the amount of cigarettes smoked for a period of at least 5 years. Pipe and cigar smokers were classified as nonsmokers.

He noted the following characteristics of smokers skin. In the crow foot, smokers wrinkles were narrow, deep and sharply contoured in contrast to the broad based more widely open round edged wrinkles of nonsmokers. These were especially evident in women. Prominent perioral wrinkles characteristic of altered dental structures were more prevalent among both male and female habitual cigarette smokers. Male smokers frequently had a characteristic pronounced cobblestone pattern to the wrinkling of the nuchal skin whether or not crows feet development was prominent. A prominent cobblestone pattern was never found in a nonsmoker.

The skin of cigarette smokers differed from that of non-smokers in color as well as in wrinkling. Among current cigarette smokers flesh-pink coloration was relatively absent whereas a yellow-gray pallor was frequently seen. Current cigarette smokers rarely had pink cheeks and almost never blushed. Ex-smokers, however, often had pink cheeks even though showing also the classical "smokers wrinkles." The study suggests a more substantial association between skin wrinkling and cigarette smoking than between wrinkling and outdoor exposure even in subjects who lived in a geographic area characterized by hot cloudless summers.

The strongest evidence supporting the conclusion is the larger percentage of heavily wrinkled individuals among the least exposed smokers of each age-sex group than among those most exposed nonsmokers of the same group. Although the pattern was repeated independently in all seven of the groups studied where prominent wrinkling was noted, the number of subjects in each classification was small and the differences were not statistically significant within any single group.

There was an association between prolonged sun exposure and increased wrinkling among smokers of both sexes but it was less striking among nonsmoking men and it did not appear among nonsmoking women. Reasons for these differences remain obscure. At present the data might be reassuring to nonsmoking female sun worshippers and should be alarming to their smoking peers. Especially of interest to obese women contemplating weight reduction is the high frequency of prominent wrinkling among smoking women who had lost over 30 lbs. This was not found among nonsmokers with a similar weight loss. Clearly a woman smoker who contemplates weight reduction should first give up her smoking habit, if she cares about her appearance.

Wrinkling of the facial skin must now be added to the list of disorders thought to be caused by smoking even though further studies will be necessary to establish the factors in the causal relationship. The association shown seems striking enough to suggest that metabolic changes induced by smoking may be a major factor in the development of wrinkles in susceptible individuals particularly when combined with habitual outdoor exposure or a large weight loss.

The association between cigarette smoking and facial wrinkling can be readily confirmed by interested even though untrained observers at any public gathering where the faces and smoking habits of individuals can be compared. In such a setting almost all strikingly wrinkled relatively young persons are seen to be active smokers.

When we inform our smoking patients that each cigarette takes away 14.5 minutes of the remaining life and that 20 cigarettes a day shortens life by 8 years, at times people remain doubters.[3] However, pointing out to a woman that her crows feet are the result of smoking should aid in communicating the personal risk of cigarette smoking to some otherwise doubting individuals.—L.H.N.

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3. Nahum, L. H.: Smoking and Physiological Age. Conn. Med., 26: 593, October, 1962.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

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CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1972 Annual Meeting of the House of Delegates is scheduled to be held in the Terrace Room of the Hartford Hilton Hotel, Hartford, on Tuesday, April 25. Commencing at 8:30 A.M. Following luncheon, the House will reconvene for the completion of its business.

Frederick C. Weber, Jr. President
Kenneth F. Brandon, Speaker of the House
Louis C. Backhus, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

MISSION POSSIBLE

THE RECIPROCAL CONVERSION OF THE "WE'S" AND THE "THEY'S"

This year's Annual Meeting of the Society will be held at the Hartford Hilton Hotel, Hartford, on April 25, 26, 27. The three-day session will include the annual meeting of the House of Delegates (April 25) and the programs of the Scientific Assembly (April 26-27).

As always, participation in the deliberations of the House of Delegates will be offered to the entire membership; first, as "observers" while the House is in formal session, and second, as active participants in the Reference Committee hearings which are held on all business of major importance. Unfortunately it must be said that, on more than a rare past occasion, it has been brought to officialdom's attention that "we" (meaning some members-at-large) are prone to take retrospective issue with what "they" (meaning the delegates) did. Reason: The "we's" were in absentia.

In similar vein, it has not been unusual to hear members attending the various programs of the Scientific Assembly (speaking as "we") observe sadly that "they" (meaning colleagues who did not attend) have missed out on excellent opportunities to further their postgraduate education.

Hence it does not seem inappropriate to urge all members of the Society to make a New Year's resolution to plan to become "they's" at the 1972 annual meeting of the House of Delegates and, conversely, to become "we's" at the 1972 Scientific Assembly. In that way, the left hand will always be able to know what the right hand is doing.

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Placement Wanted

Anesthesiology—41 years of age; Interested in large hospital; respiratory therapy and chest disease. Available early 1972. Board Certified.

Emergency Room—28 years of age. National Boards. Wishes solo or group type practice in a medium size community in Connecticut. Would consider general practice along with a small group of other doctors. Available immediately. Contact: Robert W. Lisle, M.D., 4235 Falcon Courts North, McGuire AFB, New Jersey 08641.

Dermatologist—American Board Certified; Connecticut License; Interested in Group, Associate or Institutional Practice in large or medium sized Connecticut community. 31 years of age. Nira R. Silverman, M.D., 91 Corbin Road, Hamden, Connecticut 06517.

Family Practice—28 years of age. Interested in group practice. Available mid-1972. Arthur L. Stein, M.D., 1117 Grant Boulevard, Syracuse, New York 13203.

General Practice—Connecticut license. Prefers solo practice. 50 years of age. Available immediately.

General Practice—28 years of age. Solo, group or associate practice. Connecticut license. Large or medium sized community. One year of residency in surgery. Arthur E. Woolfson, M.D., 33 Highland Street, New Britain, Connecticut.

General Practice—41 years old. Desires rural area. Solo practice. National Boards. W. Dean Pope, M.D., Box 490, Rangeley, Maine 04970.

General Practice—24 years of age. Wishes solo type practice in a small size community in Connecticut. Available early in 1972. Contact: Michael F. O'Connor, M.D., 15520 Windmill Pointe Drive, Grosse Pointe Park, Michigan 48230.

Institutional or Industrial Medicine: Solo, family practitioner in larger Connecticut community wishes to shift to institutional or industrial medicine. Board eligible. 63 years of age. Available early 1972.

Industrial Medicine—40 years of age; Connecticut and National Boards. Available early 1972.

Industrial Medicine—48 years of age; Connecticut license; Presently with firm in New Jersey. Wishes to relocate. Available immediately.

Internal Medicine—34 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut, in a medium size community. Connecticut license. Available immediately.

Internal Medicine—31 years of age, Certified, wishes group type practice in a medium size community in Connecticut. Available immediately.

Internal Medicine—Cardiology—34 years old; To relocate in Connecticut F.R.C.P. (C.). Eligible with National Boards. Desires hospital based or group practice position. Available immediately.

Internal Medicine—36 years of age; National Boards; Board eligible; Group or Associate practice; Available immediately.

Internal Medicine—62 years of age. Wishes solo or institutional type practice in Connecticut. Board Certified. Available immediately.

Neuropsychiatry—48 years old; Connecticut License in process. Solo, group, associate, institutional. Interested in E.E.G. Experience in research and teaching. Andre J. Angyan, M.D., Ph.D., 321 Orchard Drive, Pittsburgh, Pennsylvania, 15238 (412-828-5509).

Ophthalmology—30 years of age; National Boards, Board eligible; solo or associate type practice. Available March 1972.

Ophthalmology—31 years of age; Board eligible: National Boards; Solo or associate type practice.

Pathology—33 years of age. Connecticut license. Board Certified. National Boards. Presently in practice. Wishes group or associate type practice. Available immediately.

Pathology—46 years of age; Board certified; Prefers medium size community; Connecticut License; Available February 1972.

Radiology—42 years old; Board Certified; FLEX; Presently teaching. Available immediately.

Summer Employment Opportunities: Camp physicians; part time or vacation coverage. Medical students seeking hospital or laboratory positions. Contact: Connecticut State Medical Society—203-865-0587.

General Surgery—41 years of age. Certified. Presently in practice. Wishes group or associate type practice in a medium or small size community in Connecticut. Available in January 1972. Please contact: Jose Peralta, M.D., 1916 Grand Concourse, Bronx, New York 10457.

General Surgery—32 years of age. Eligible with Connecticut license. Wishes group, associate or institutional type practice in Connecticut. Available immediately.

General Surgery—32 years of age; Board eligible; small or medium size community; solo, group or associate practice. Available immediately.

Placement Opportunities

Allergist: Wanted immediately to take over active practice and office; medium size (70,000) Connecticut community. New Haven area. Annual gross $58,000. Sole allergy practice in area. Call (203) 735-9501.

Allergist—Associate practice in larger Connecticut community.

Connecticut Based Insurance Company: Three physicians needed: Employee Health Clinic; Claims Review; Medical Evaluation for Underwriting Purposes. Connecticut license. Good benefits.

Anesthesiologist—To join Board-certified chief of anesthesiology in small community hospital. No OB. Salary negotiable. If interested contact administrator or chief of anesthesiology. Johnson Memorial Hospital, Stafford Springs, Connecticut 06076.

Family Practice—Southwestern Litchfield County. Community hospital. Conveniently located. Community physicians also searching for pediatrician and Ob/Gyn to enter private practice.

Family Practice—Growing community seeks family physicians. North-central Connecticut. Approximately 47,000 population. Several hospitals in the area. New hospital in planning stages. Number of specialists in town. Conveniently located.

Associate in General Practice: Busy general practice in Milford, Connecticut including pediatrics, Obstetrics and Gynecology, and some surgery (major and minor). New fully equipped office across the street from 200 bed open staff hospital. Boating, fishing and beaches 5 minutes from office. Yale-New Haven Medical Center and Yale cultural facilities 15 minutes away. Salary for one year with partnership to follow if agreeable. Please contact: Barry M. Winters, M.D., 73 Golden Hill Street, Milford, Connecticut 06460.

General Practitioner Preferred—Will involve travel to medicare facilities and review patient care standards. Travel to 30% nationally in one-two week spans. Salary to $30,000. Fee Paid. Contact: F-O-R-T-U-N-E Personnel, 60 Washington Street, Hartford, 547-0900.

Director of Mental Health Training in a 1500 bed psychiatric hospital: dynamically oriented-unit system; progressive team approach; association with Yale University Departments of Psychiatry and Neurology. Directs the Psychiatric Residency training program, providing intensive training and experience with individual supervision in all psychiatric modalities; arranges visiting lectures and seminars. Opportunities to develop new programs for training and education in multidisciplinary areas. Board certification in psychiatry; eligibility for state licensure; administrative ability and teaching experience necessary. Salary commensurate with experience and training, liberal benefits, including free hospitalization. Please send resume and particulars to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut, 06457.

Director of College Health Service—Full time position; September, 1972; C. B. Crampton, M.D., Wesleyan University, Middletown, Connecticut 06457.

General Medicine and Internal Medicine—Northwestern Connecticut community seeking to attract practitioners. Associate type practice possible.

Ob/Gyn—Community in western Connecticut in search of physician to open private practice. Community's growth requires additional medical services.

Occupational or Industrial Medicine—Two Connecticut post offices need staff physicians. Connecticut license. Part or full time.

Orthopedic Surgeon—Central Connecticut area. Community Hospital. Group practice with three other orthopedic surgeons.

Pediatrician—Community physicians feel that another pediatrician is needed. Central section of the state. 40% of population 18 years of age and under.

Pediatrician—currently board-eligible or board certified. Full-time position. Salary negotiable. To practice family oriented medicine in a private, non-profit neighborhood health center. For further information please contact Evans H. Daniels, Jr., M.D., Medical Director, Community Health Services, Inc., 1023 Albany Avenue, Hartford, Connecticut, 06112. Telephone 549-1423.

Urology—Interested in an associate. Large, Southwestern Connecticut shore community.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

news from the

Connecticut Regional Medical Program

On December 13, 1971 Dr. Harold Margulies, Director of the Regional Medical Programs Service, advised CRMP that its triennial grant application had won the endorsement of the National Advisory Council and been recommended for funding at the following levels: $2,097,037 for 1972, $2,332,820 for 1973, and $2,500,000 for 1974. (All direct costs).

At the same time Dr. Margulies advised CRMP that, owing to federal budget limitations, the actual award to CRMP for 1972 would be $1,447,316. Since that communication, however, CRMP has learned that some additional funds may be released to RMPS for program support in 1972, and CRMP will follow whatever procedures are established to qualify for additional funds.

As a result of the reduced grant award for 1972 the CRMP Advisory Board on December 14 approved the assignment of funds based on the following criteria: continue support at 1971 level for on-going program elements where personnel are currently functioning; support to maximum possible the central thrust of CRMP, i.e., Community Studies Capability, University and Community Based Regional Faculties, Core Staff; no funding for new program elements for 1972 or expansion of old ones except those related to the central thrust. In making this judgment the Advisory Board recognized that supplemental support for 1972 may develop, including categorical grants for kidney disease, area health education centers, health maintenance organizations.

Meanwhile, it may be of interest to Connecticut's physicians to learn what assessment the national site visitors, RMPS staff, and the National Advisory Council have made of CRMP after three years of operation. In his "Advice Letter" Dr. Margulies stated:

"On the whole, the Council is impressed with the progress being made in Connecticut. The cornerstone of your program development, full-time chiefs of service, backed by university resources, is developing well. Not only have the number of full-time chiefs increased markedly, with undoubted benefits to hospitalized patients, but benefits also to ambulatory patients and the community are beginning to occur. The community outreach is considered by our reviewers as an important index of your program's flexibility and capacity to respond

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to problems that have emerged since the design was outlined or were not recognized by the initial combination of provider and consumers involved in the planning and development of the Connecticut program. It is an area that the reviewers feel needs considerably more time and attention by the Connecticut Regional Medical Program in the next triennial period."

Dr. Margulies went on to state: "The reviewers were pleased to note that the CRMP has contributed successfully to several activities now receiving continued support from other sources. The two clinics—Middlesex and Community Health Services Inc. —, the planned phase-out of RMP support for full-time chiefs of staff, and the appointment of full-time chiefs with no RMP support were considered positive indications of the program's ability to initiate well conceived activities that are subsequently supported from other sources."

The work of the CRMP Review and Evaluation Committee drew favorable comment. "The Council commends CRMP for the imaginative utilization of the Review and Evaluation Committee. Not only does this Committee provide on-site evaluation of program activities, it serves as a resource to the Executive Committee and Advisory Board in making funding priorities. The reviewers believe that the addition of staff to the evaluation process would further strengthen program evaluation."

In the area of recommendations, Dr. Margulies cited the need for further development of outreach activities related to primary care, additional sources of support for the university-based regional faculty, increased core staff, more effective minority representation on the Advisory Board, and improved communications and liaison with comprehensive health planning, with CSMS, with allied health organizations and the general public.

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Management of high-risk pregnancy and intensive care of the neonate. S. Gorham Babson, M.D. and Ralph C. Benson, M.D. Second Edition. The C. V. Mosby Company, St. Louis, 1971. 301 pp. with 62 illustrations. $16.50.

Speech Pathology. An applied behavioral science. William H. Perkins, Ph.D. The C. V. Mosby Company, St. Louis, 1971. 430 pp. $11.75.

NEW BOOKS IN REVIEW

ENERGY METABOLISM IN TRAUMA. A Ciba Foundation Symposium: Edited by Ruth Porter and Julie Knight. Published by J. & A. Churchill, 104 Gloucester Place, London, 1970. 202 pages, 60 illustrations.

Reviewed by: C. FRANCIS ROE

This volume consists of papers presented to the Symposium on Energy Metabolism in Trauma in February, 1970. This symposium, held under the auspices of the Ciba Foundation, was under the distinguished chairmanship of Dr. Hans Krebs, and brought together clinicians, physiologists and biochemists from the U.S., Great Britain and other European countries. As with many such symposia, it is difficult to detect a trend or pattern from the papers presented, but two broad areas of research seemed to emerge. One dealt with the general effects of trauma on energy expenditure and the mechanisms for maintaining energy balance, and the other dealt with the biochemical alterations in the functions of different enzyme systems caused by trauma. Perhaps more emphasis was placed on such subjects as intermediary carbohydrate, protein and fat metabolism in trauma. The chairman suggested, in his summing-up, that this was the area where most progress was to be made in the future, but the papers presented on these subjects did not appear to bear this out. Little that was new or unexpected came out of this part of the symposium, whereas in the area of overall energy metabolism, the study of the physiological responses to trauma offered new insights into the basic mechanisms which underlie the biochemical alterations. A problem common to much surgical research arose during this symposium; to what extent can laboratory animal data be extrapolated to the human situation? In this instance, it is evident that the traumatised rat behaves in a quite different physiologic manner from the human; changes in oxygen consumption, body temperature and other parameters may occur in opposite directions from those seen in man. This leads one to regard laboratory animal data on trauma with more than usual suspicion from the point of view of applicability to man, and nowhere is Pierre Charron's dictum that "the true science and the true study of man is man" more true. In one or two instances, material presented in this symposium was merely a rehash of long-since moribund work, but on the whole presented a fair overview of the state of the art in this awakening area of endeavour.

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Special Article

Medical Progress A Century Ago: The Physiology Laboratory Comes To America*

Part II

Hebbel E. Hoff, M.D., Ph.D.

The winds of change in medical education that blew so strongly in Harvard in 1871, as described in the first of this series, had their origin in the founding of the University of Berlin in 1809. As Flexner described it, "on the founding of the University of Berlin new wine was poured into the old bottles; and the old bottles burst. Never before or since have ancient institutions been so completely remodeled to accord with an idea." What was the idea and how did it come about?

Just then Germany was helpless; it lay splintered into small states, prostrate under the armies of Napoleon, its Universities were centers of medievalism and its other institutions almost as archaic. But Kant, Leibnits, and Goethe had had pioneered in Philosophy, Mathematics, and Natural Science and their successors fitted together the elements of the German resurgence of the 19th century. From Hegel (and Fichte and Schilling), came the restatement of the Cusan doctrines of the idea of the slow approach toward an unattainable perfect truth by slow and painful steps, and the reconciliation of opposites through religious insight. According to Hegel, spirit (geist) constitutes the unity in which contradictions such as finite and infinite are embraced and synthetized. To him the problem of the modern world is to construct an order which satisfies the rival claims of universal law and individual conscience. From him came the philosophy of the unified state as the embodiment of reason, and Hebbel in his most powerful work, Agnes Bernauer, made the inevitable clash between the necessities of the state and the rights of the individual its central theme. It still continues to be so today, not totally without value in the mind of Scheiermacher, another founder of the University of Berlin who saw all knowledge as a product of the conflict of thoughts.

In this intellectual atmosphere there developed an unusual administrator, Wilhelm von Humboldt, who conceived the salvation of Germany in the powerful combination of teaching and research. At that time and most particularly in Germany, teaching was centered in the Universities while research had largely fallen to the academies, modelled most particularly on the Royal Society of London and the Academy of Science in Paris. Here the "new philosophy" of the search for new knowledge wherever it was found, and its application to the practical needs of society were especially cultivated, and the idea of Journals for the rapid dispersal of knowledge was developed. (The first accounts of blood transfusion appeared in the Philosophical Transactions of the Royal Society on November 19 and December 17 of 1666; the first experiments in Paris, derived from these reports, began on January 22, 1667). It was von Humboldt's success in achieving the synthesis of what many people then considered to be the conflicting functions of teaching and research (some still do) that created the revolution in the function of the University that Flexner referred to in the first paragraph. It should never be forgotten that the "Academic" function

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DR. HEBBEL E. HOFF, Benjamin F. Hambleton Professor and Chairman, Department of Physiology, and Associate Dean for Faculty and Clinical Affairs, Baylor College of Medicine, Houston, Texas. Consultant in Physiology, U. S. Veterans Administration Hospital, Methodist Hospital, Houston, Texas.

* *Supported in part by USPH-LM00453-04 from the National Library of Medicine.*

of a University, introduced at this time and in this way, refers to (1) the search for new and more complete knowledge, and (2) the duty to apply the new knowledge to the needs of society.

The system von Humboldt devised for administration of the University contained two vital elements from which certain corollaries naturally derived. The first was the professor's freedom to teach his subject as he wished and the student's right to learn what he wanted and as he wanted; in both cases it was the results that counted and not how it was accomplished. These were the fundamental principles of Lehrfreiheit and Lernfreiheit of the German universities which, however much they have been circumscribed, hedged, and arbitrarily disregarded since then, remain the benchmarks of good university practice.

The second principle was that of peer selection of Professors. Committees of faculties were set up to review the field, not only nationally but internationally (in actual practice this was largely restricted to the German speaking world, but that included Switzerland and the Austrohungarian Empire). The usual practice was for the faculty to make three nominations and for the Minister of Education to make the final selection from these three. This of course is not far from the American practice which substitutes the Board of Trustees for the Minister of Education, and of course this created another conflict that made possible many abuses—the remarkable scientist Remak could never be confirmed in a professorship because he was Jewish and he had to move out of the University into practice, the brilliant promise of his early years unfulfilled.

The natural result of the application of these two principles was the resulting mobility of professors and students. Professors moved from the smaller and less prestigious schools to those with greater facilities and greater fame, but although there was a natural movement of some of the best professors to Berlin, the University of Berlin never held quite the paramount position of that in Paris, for example, or of Oxford and Cambridge in England. Willy Kühne to cite one example, was more than content to remain in Heidelberg despite tempting offers from Berlin, and Carl Ludwig remained attached to his Institute in Leipzig. Thus the University of Berlin served as a model for the rest of the German speaking world instead of a too-powerful magnet, and acting on its principles other universities developed in its light and not in its shadow.

Students moved freely too, the wandering scholars of medieval times persisting in Germany longer than in any other country. Their migrations were encouraged by the frequent moves of the professors, whose loyal students followed them; as well as by the development, also from a medieval model, of the Privatdozent, a teacher below the Professorial rank who was enpowered to give courses for fees. Some of these gained great popularity and had large followings of students who would migrate from university to university to follow popular courses. This idea never attained any great popularity outside of Germany, and has by now lost much of its attraction in Germany itself.

Despite its imperfections, and perhaps because it brought opposing ideas into conflict and so exercised a forcing function on discovery and innovation, the system worked, and by as early as 1825 according to some students, the center of gravity in mathematics had shifted to Germany to take its place beside Philosophy, which was already there. Then, as Osler wrote, the Muse of Medicine began to shift, more slowly, because it was well entrenched in Paris, but inevitably as the critical mass and the pluralist approach of the many German university centers inevitably outweighted the French system which concentrated its main effort in Paris.

Among the greatest of the German Physiologists for his contributions to the science was Carl Ludwig, but when considered from the standpoint of the School he developed, the pupils he taught, and the influence they have exerted on the progress of Physiology throughout the world, he was without a peer, and most perfectly exemplified the combination of teaching and research, and the mutual reinforcement they exert on each other. His pupils and their students down to the fourth and fifth generations represent practically the whole family tree of Physiology today: Adolf Fick of cardiovascular fame; *his* pupil Jacques Loeb came to America to found his own great school; Christian Loven came from Sweden; Tiegerstedt was his pupil. Christian Bohr founded the great Danish school of Physiology, Sechenov and Pavlov brought Ludwig's school to Russia, Michael Foster and Schaefer did the same for England and Adrian and Sherrington were their pupils. Chittenden, Lombard and Bowditch propagated his school to America, as did Mosso and Luciani for Italy.

Carl Ludwig was born in 1816, son of an army officer retired because of injuries in the Napoleonic wars, and studied medicine at both Erlanger and Marburg, graduating in 1839 at the age of 23. In this small town some 60 miles north of Frankfort am Main, and in its university which had been the first Protestant University to be founded in Europe (1527) and where Luther had formulated the 15 articles of the Marburg Colloquy which stated the common doctrine of the German and Swiss Reformation, Ludwig continued to develop, first as Privatdozent and then as Professor of Comparative Anatomy. Here in the years before 1847 he put together, from complicated sources in meteorology, ballistics, hydraulics, etc., the remarkable instrument he called the Kymograph, by which a physiological event so to speak wrote out its own activity on the smoked paper of a revolving drum, and which became the mainstay of physiological investigation and teaching for more than three quarters of a century, when it was gradually replaced by the technology of the modern world. The principle of graphic recording of bodily functions has remained valid, and has developed into a principal tool of study of human function in health and disease.

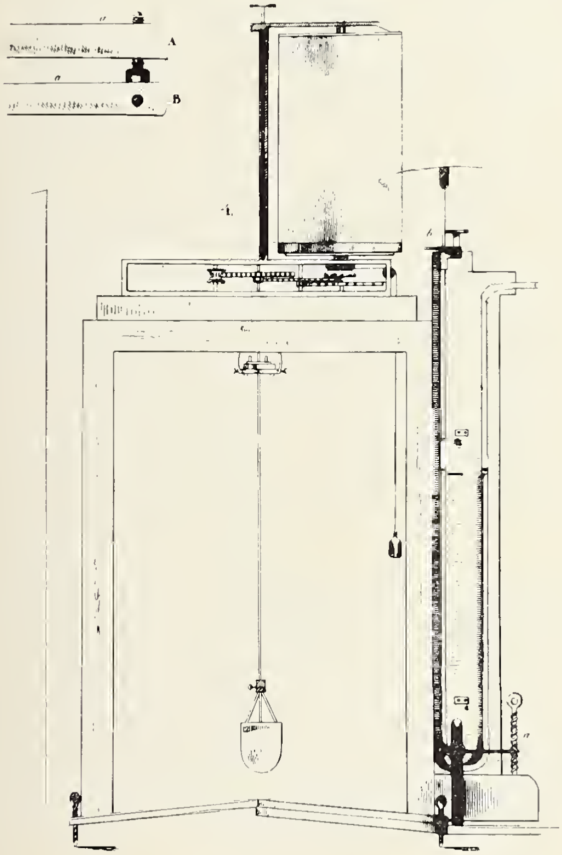

Figure 1

Ludwig's original Kymograph as described in Archiv. f. Anat. u. Physiol., 1847, p. 261 et. seq. It shows on the left the rotating smoked drum driven by a clockwork mechanism powered by a falling weight. To the right is the mercury manometer to be connected by a cannula and appropriate tubing to the carotid or femoral artery. A float on the open arm of the manometer at the left carries a stem and stylus which write out the oscillations of the mercury manometer produced by the beat by beat changes in blood pressure.

In 1865 Ludwig was fifty, he had transferred from Marburg to the Chair of Physiology and Anatomy in Zurich, and from there he had gone to the Chair of Zoology and Physiology at the Academy for Military Surgeons in Vienna, where he stayed from 1855 to 1865. Then he made his final move to the Physiological Institute in Leipzig, where he remained as active Director until his death at the age of 79. It was here that with growing acclaim, his Institute became the center for research and teaching in Physiology and the source of the predominant blood lines of physiologists throughout the world.

To this Institute in 1869 there came Henry Pickering Bowditch. Son of a Boston merchant and grandson of Nathaniel Bowditch, author of the *New American Navigator,* Bowditch had left his studies at the Lawrence Scientific School in Cambridge to join up as First Lieutenant in the 1st Massachusetts cavalry. He served throughout the war, from November 1, 1861 to June 3, 1865 being discharged as Major in the 5th Massachusetts cavalry. Completing his course at Lawrence, he was admitted to Harvard Medical School, completed the two required years of course work described in the last article, and received his M.D. in the spring of 1868. By summer he was in Paris attending Claude Bernard's courses, studying microscopy from Ranvier, and following the wards rounds and amphitheater clinics of Charcot. A chance meeting with Willy Kühne led Bowditch to Ludwig's laboratory in September of 1869 where he derived "the formative and directive stimuli which were to determine his subsequent career."

Bowditch was attracted to and soon became an adept in the electromechanical operation of Ludwig's Kymograph as a research instrument; he is credited with contributing the idea of using an electromagnetically driven pendulum to generate the timing signals on the revolving smoked drum. He became interested in recording the beats of the isolated frog heart and established the law of "all or nothing". In addition he described the phenomenon of "Treppe" and closely approached the idea of the refractory period which Marey would later develop more completely.

After a first invitation from Charles Eliot, which he rejected because he wished to continue his studies with Ludwig, Bowditch accepted Eliot's second challenge to return to Harvard Medical School to "take part in the good work of reforming medical education." He returned to Boston in September of 1871 ready to give the first course in Physiology under the new curriculum at Harvard. Here, with apparatus acquired in Leipzig he started the first physiological laboratory in this country. Before long there were other laboratories at Michigan under Lombard, at Johns Hopkins under Newell Martin, both students or descendants of Ludwig, and eventually they were in all medical schools and many universities, often using the ingenious apparatus designed at Harvard by Bowditch and his faculty. (Lombard was also skilled in the design of apparatus for the physiological laboratory and this in general has proven to be an inheritance of most of Ludwig's descendants).

At Harvard, Bowditch continued to teach Psysiology and encourage research for 35 years, generating a numerous progeny of American physiologists, including in the earlier years William James and Stanley Hall and at the turn of the century Walter B. Cannon, whom he brought in as a junior medical student to help in the pioneer work on radiography out of which grew Cannon's classical studies on gastric motility.

While in Leipzig Bowditch wrote an account of Ludwig's Institute which was published in the Boston Medical and Surgical Journal in 1870 (new series, vol. 5: pp. 305-306). It was sufficiently interesting to the English speaking world to be reprinted first in Nature (Dec. 22, 1870) and finally in the Lancet on January 14, 1871, in a condensed form. The influence of this short note on the development of laboratories of Physiology throughout the world makes it still worth reading:

> "An interesting account of the Physiological Laboratory at Leipzig is given in the last part of of our contemporary *Nature*, the editor of which we have to thank for obligingly lending us the accompanying ground-plan. The description of the laboratory, which we have here condensed, has been forwarded by Mr. Bowditch, who is at present working in it.

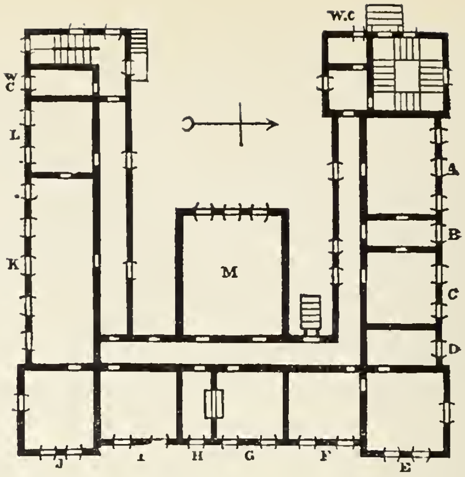

Figure 2

Bowditch's sketch of Ludwig's Laboratory of Physiology in Leipzig.

> "The Building owes its existence to the energy of Prof. Carl Ludwig and to the liberality of the Government of Saxony. It is of the shape of the letter E: the small projection in the center being the lecture-room; the north and south sides having a length of 119 feet, and the east side of 122 feet. The right wing of the building constitutes the microscopical department, the left the chemical department of the laboratory; while the central portion is devoted to the study of experimental physiology in the narrower sense of the word. Thus the room A is arranged for the accommodation of beginners in the study of microscopy, with every requisite. Room B is the private study of the assistant in microscopy. Room C is intended for more advanced students in microscopy; and contains an injecting apparatus, by means of which three different fluids can be injected simultaneously under any required pressure and for any length of time, while the injection-mass and the tissue to be injected are heated over a warm bath. Room D contains a small library, consisting of such books as are most needed for reference. Room E is furnished with glass cases, in which physiological apparatus is kept when not in use. As a rule, no experiments are performed in this room. Rooms F, G, and H are devoted to experimental physiology, and are furnished with operating tables, with bellows attached for keeping up respiration in curarized animals, registering apparatus of various sorts for recording the pressure of the blood, water-baths, an injecting apparatus, evaporating closets, etc. Between rooms G and H is a small closet arranged for observations with the spectroscope. Room I is the chamber where all experiments are performed requiring the use of large quantities of quicksilver. It contains the quicksilver pumps for extracting gases from fluids, and instruments for measuring the activity of the respiration in man and the lower animals. Room J is divided into two portions, one of

which is used for a weighing-room, and the other for experiments in acoustics. Rooms K and L contain, besides the ordinary furniture of chemical laboratories, the ingenious air-pump of Bunsen by which the process of filtering is so greatly accelerated. The lecture-room M presents every accommodation for 100 students. In the basement of the building is a small gas engine of about one horse-power, which drives the respiration apparatus, registering instruments, etc. In the basement are also the rooms where the animals are kept (one room being entirely devoted to frogs); a chamber with refrigerators and another with furnaces. The second story of the building is occupied by Professor Ludwig and his family and the resident assistants. In the court-yard are the necessary arrangements for experimenting on horses and other large animals, an aviary, and a fish-pond. The laboratory is kept well supplied with new instruments for special research, and a skillful mechanic lives on the premises.

"The number of pupils is nine at present, and each undertakes, under the direction of Ludwig a series of experiments, with the view of settling some special point in physiology, the results being annually published in a report from which we have frequently quoted. All expenses, down to the frogs, are borne by the Saxon Government. Surely this is very creditable to that little State, and we warmly recommend this establishment to the University of Cambridge as a model on which they may construct, with what improvements their able and newly appointed Professor can suggest, the buildings it will be absolutely necessary to raise, if physiological science is ever to be taught with the same advantages as those which are readily accessible to every earnest student on the Continent."

(This is the second of a two-part series)

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APRIL 25, 26, 27, 1972

PLAN NOW AND SAVE THE DATES

Electrocardiogram of the Month:

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Normal Variants Mistaken as Evidence of Heart Disease
I-ECG Mimic of Inferior Wall Infarct

To prevent heart disease of electrocardiographic origin it is necessary that the reader be aware of the variants simulating ischemic heart disease and that the heart be considered to be innocent until proven guilty.

It is not uncommon in normal subjects of tall and slender body habitus whose hearts on X-ray show a "drop" shape appearance for the electrocardiogram to exhibit Q waves preceding the R waves in leads 2, 3, and aVF, and downward slope of the ST segment terminating in inverted T waves in these same leads (Fig. I). T wave inversion may also be seen in lead V6 especially if the chest electrode is placed one intercostal space lower than usual. It is this finding of Q waves and inverted T waves in these leads that often leads to the mistaken diagnosis of previous inferior wall infarction. To avoid such misinterpretation one must apply rigid criteria for the diagnosis of *abnormal* Q and T waves in these leads. The normal physiologic Q wave present in leads 2, 3, and aVF when the heart is in a vertical position is narrow, usually less than 0.025 second in duration, is not slurred, and it is of low voltage, the ratio of Q amplitude to R amplitude in lead aVF being considerably less than 1:4. In contrast the abnormal Q wave in leads 3 and aVF caused by previous infarction of the inferior wall is usually 0.035 second or more in duration, is often slurred, and its amplitude is usually more than 25% of the R amplitude in these leads. The inverted T waves appearing as a normal variant in leads 2, 3, and aVF are usually asymmetrical whereas the inverted T waves caused by previous infarction of the inferior wall tend to be symmetrical (Fig. II).

At times the differential diagnosis may be difficult because the abnormal Q wave resulting from may decrease in amplitude and duration in the course of its evolution. If, however, there is no such history of previous infarction and there are a previous well documented inferior wall infarct no other findings in the 12 lead tracing it is unwise to rely solely on the electrocardiogram for diagnosing the presence or absence of heart disease.

Misinterpretation of electrocardiographic findings as noted above should be rigorously avoided since it often leads to unnecessary hospitalization, unnecessary restriction of physical activity and refusal of life insurance. It may also create dire psychological consequences when a healthy person is labelled a "cardiac" on the basis of electrocardiographic interpretation alone.

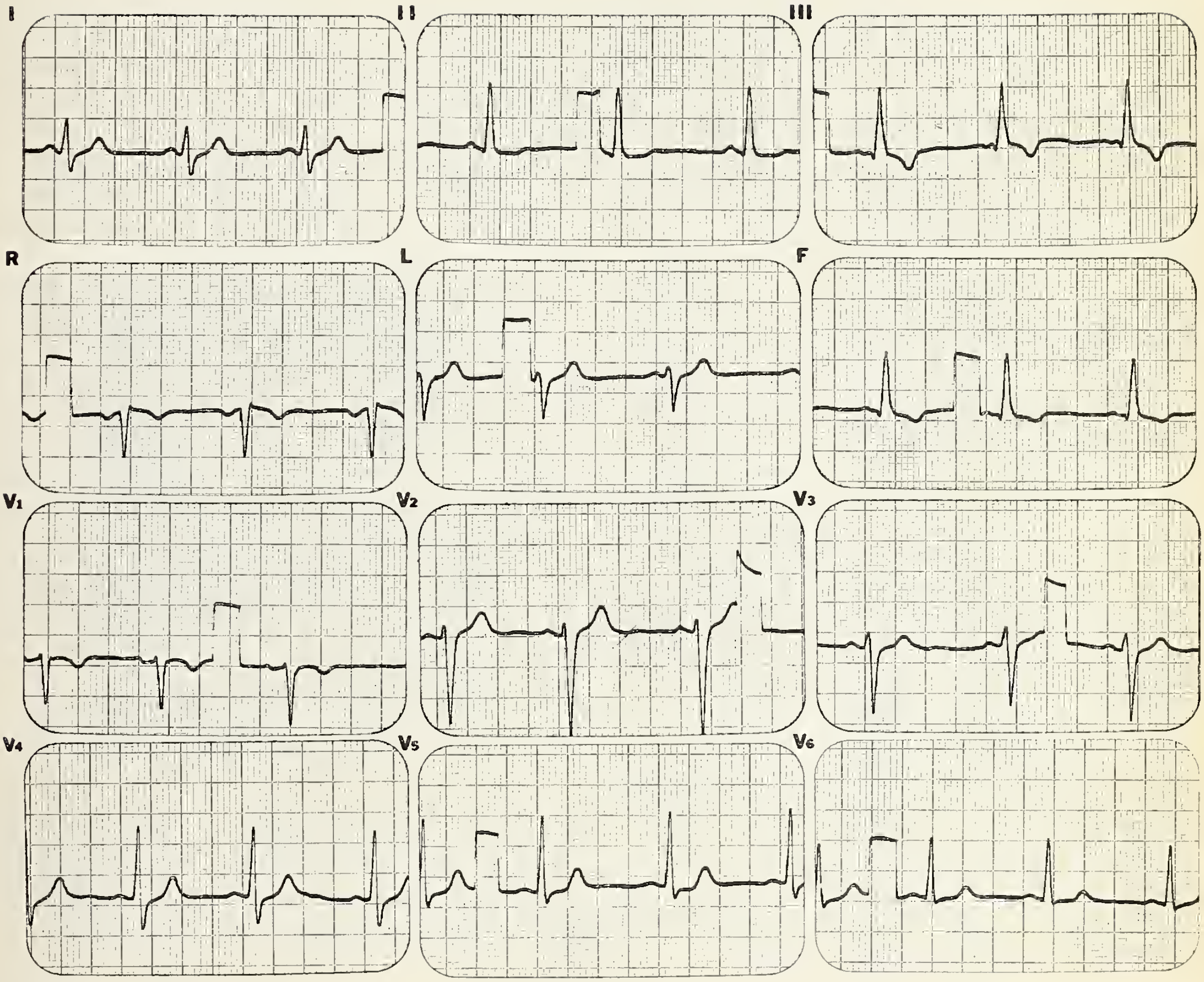

Figure 1
Electrocardiogram of female, age 18. Height 72 inches. Weight 120 pounds. No clinical evidence of heart disease.

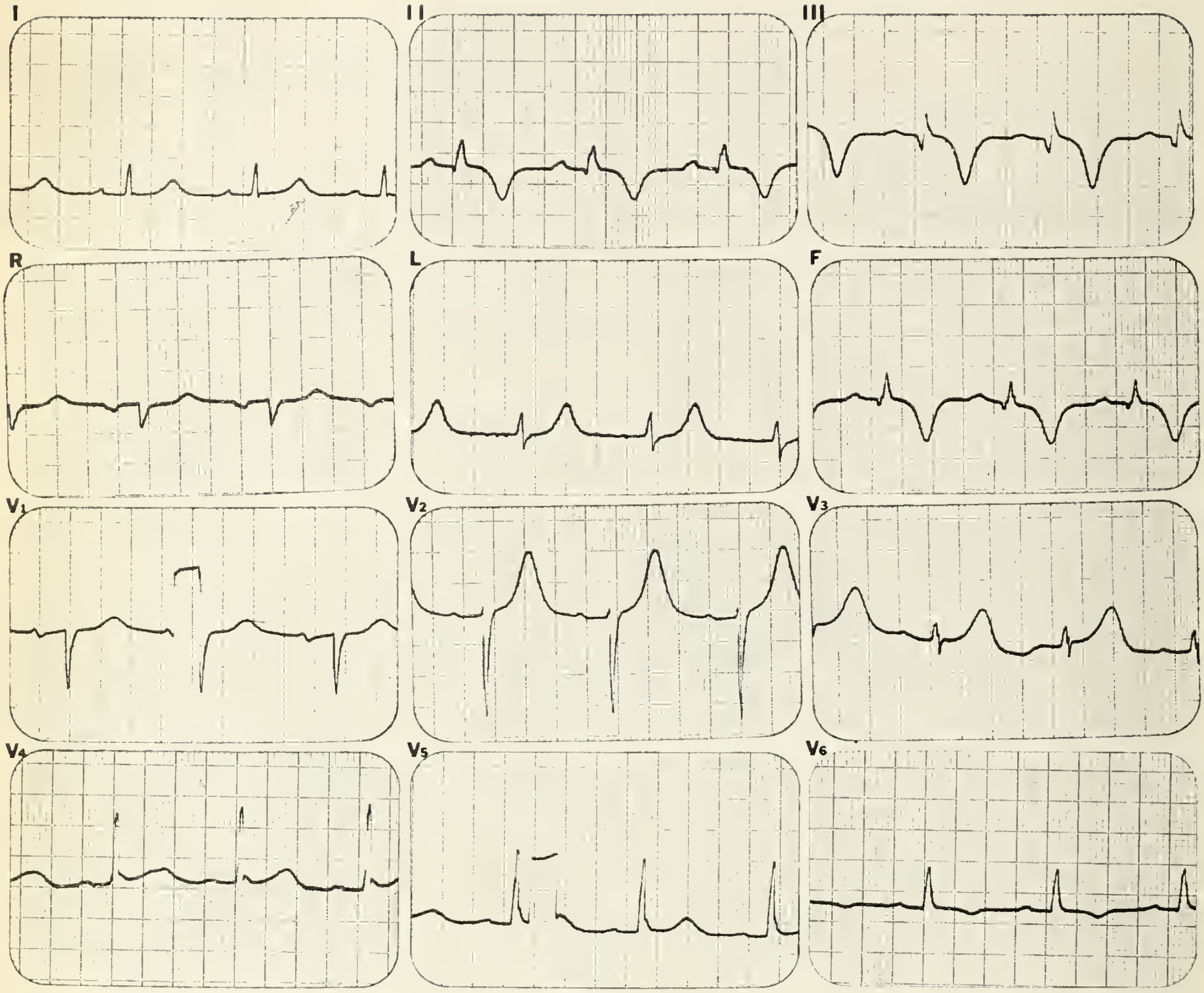

Figure 2

Electrocardiogram of male, age 54. History of infarction of the inferior wall 2 years prior to the recording of this tracing taken prior to contemplated gall-bladder surgery.

OBITUARY

Nathan M. Winick, M.D.
1914-1971

Dr. Nathan Winick was born in Bayonne, N.J., May 21, 1914 and died October 14, 1971. He moved to Hartford in his early life and attended local schools. He received his undergraduate and medical degrees at New York University. He was elected to A.O.A. in his junior year at medical school. He interned at St. Francis Hospital in Hartford where he also served a residency in Pathology.

His further training was obtained at Montefiore Hospital and the New York Post-Graduate Hospital where he became a right hand to Dr. Charles Gordon Heyd. He followed his surgical training at Post-Graduate Hospital with residencies at the Westfield State Sanatorium and the Lawrence and Memorial Hospitals. He was certified by the American Board of Surgery and was a member of the Hartford County Medical Association, the Connecticut State Medical Society and the American Medical Association.

Desiring to be close to his parents he returned to establish a surgical practice in Hartford. From the beginning of his practice he was affiliated with Mt. Sinai Hospital and the St. Francis Hospital. He served as a surgeon on the staffs of Westfield State Sanitorium in Westfield, Mass. and Lawrence and Memorial Hospital in New London. He became associate in general surgery at Mt. Sinai Hospital. He also devoted many hours of loyal service to the patients of the McCook Memorial Hospital while on that staff.

He loved surgery but was ever restrained and conservative in the use of the scalpel. He sought frequent consultation mindful of the welfare of his patient above all else. He was scrupulously ethical in his professional life. His was an analytical mind ever investigating unexplained data. He served on the Executive Committee of Mount Sinai Hospital with devotion. He was devoted to the opera and loved music. His knowledge of world literature was unsurpassed.

In his loyalty to his patients he was frequently misunderstood taking the slightest deviation from the highest standard of medical practice as a personal threat. He was gentle and warm when consolation and understanding were essential. He used his fluency in Spanish to lighten the heart of many an unfortunate patient who was a stranger to the English language.

To the end of his days he worried about every single patient who was critically ill. He died at his desk with an open book symbolic of his intellectual life. He will ever be remembered by those who were privileged to know and work with him and call him friend.

He leaves his parents, William and Sarah Wagman Winick of Windsor; and two brothers, Fred Winick of West Hartford and Louis Winick of Miami, Florida.

Gerald I. Pitegoff, M.D.

In Memoriam

Fekety, Stephen, Tufts Medical School, 1930. Dr. Fekety was an orthopedist in the Middletown area since 1931. He died December 2, 1971, at the age of 67. He was a member of the Middlesex County Medical Association, Connecticut State Medical Society and the American Medical Association.

Foster, Edward W., Harvard Medical School, 1924. Dr. Foster was a practicing surgeon in the Meriden area since 1929. He was a member of the Founders' Group associated with the inception of World War II Veterans Memorial Hospital and served as that hospital's first chief of surgery in 1954. Since then he continued to be active as a member of the medical and surgical staffs. During World War I, he served overseas in the U.S. Army Medical Corps. Dr. Foster was on the surgical staff of Meriden Hospital, serving in various staff positions. He was a consulting surgeon and in September of 1971 was appointed to the Emeritus Staff of the Meriden-Wallingford Hospital. He was a member of the Meriden-Wallingford Medical Society, a former officer of the New Haven County Medical Association and a member of the American Medical Association. Dr. Foster died December 22, 1971, at the age of 77.

Gildersleeve, George H., Yale University School of Medicine, 1923. Dr. Gildersleeve was a surgeon in the New London area since 1925. He served with the U.S. Navy during World War I and for more than 30 years was affiliated with the Connecticut Public Health Council. He resigned the post of medical examiner which he held for many years, when he became hospitalized in November. He was a member of the New London County Medical Association, the Connecticut State Medical Society and the American Medical Association. He also served as president of the Connecticut State Medical Society in 1953. Dr. Gildersleeve died December 22, 1971, at the age of 73.

Murray, Henry J., Jefferson Medical College, 1916. Dr. Murray was a practicing otolaryngologist in the Fairfield area since 1916. During World War I he served in the U.S. Navy as Lieutenant, M.C. Dr. Murray was a member of the Fairfield County Medical Association, the Connecticut State Medical Society and the American Medical Association. He died October 27, 1971, at the age of 79.

Tarasovic, Thomas J., Tufts University, 1936. Dr. Tarasovic was a practicing physician in the Fairfield area since 1936, and was the plant physician and head of the medical staff and plant hospital facilities at Avco Lycoming Corp. in Stratford. Dr. Tarasovic was a member of the Fairfield County Medical Association and served as treasurer and member of the board of trustees. He was also a member of the Connecticut State Medical Society and the American Medical Association. Dr. Tarasovic died December 12, 1971, at the age of 60.

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Meeting Notices

The information on this "notices" page is offered as a service of all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the month preceding, date of issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

GENERAL

April 25-27, 1972—Tuesday-Thursday
180th Annual Meeting of the Connecticut State Medical Society
Theme: Clinical Pharmacology
Hartford Hilton, Hartford

September, 1971-May, 1972
Lecture Series—Each Tuesday
Basic Sciences As Related to Clinical Medicine: Infectious Diseases, Coronary Care Problems, Diagnosis and Treatment of Tumors
Lawrence and Memorial Hospitals
New London, Connecticut
Contact: Edward Gipstein, M.D.

February 27-March 1—Sunday-Wednesday
The American Fertility Society's Fifth Postgraduate Course and 28th Annual Scientific Meeting
The Waldorf-Astoria Hotel, New York City

March 20-24—Monday-Friday
Specifically Treatable Diseases
University of Pennsylvania School of Medicine, Philadelphia

ENDOCRINOLOGY

March 7-10—Tuesday-Friday
Advances in Clinical Endocrinology
Boston University Medical Center,
Boston, Massachusetts

SURGERY

February 2-5, 1972—Friday-Saturday
Symposium on Problems of the Female Breast as Related to Neoplasms and Reconstruction
Memorial Sloan-Kettering Cancer Center,
New York City

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American Medical Association—Education and Research Fund

Established in 1951, AMA-ERF seeks financial support from the nation's physicians, medical societies, woman's auxiliaries, philanthropic organizations, business corporations, and the general public.

There are three facets of the AMA-ERF for which the National Woman's Auxiliary actively seeks funds—the fund for Medical Schools, the Student Loan Guarantee Fund and the Institute for Biomedical Research. The need for funds for medical students is well-known to doctors and their families. Medical schools need flexible financial aid—money without strings attached to use as they see fit to solve their most pressing problems. Contributions may be designated for a particular school, or donated to the general fund for medical schools which is equally divided among all accredited schools at the end of the calendar year.

Funds collected in 1970 and distributed to Connecticut's schools are as follows:

	Earmarked	*Undesignated*	*Total*
Yale Univ. School of Medicine	$1,869.49	$2,719.61	$4,589.10
Univ. of Conn. School of Medicine	$741.50	$2,719.61	$3,461.11

Contributions for the above can be made through direct mailing of check to the County chairman of the Woman's Auxiliary AMA-ERF committee and may designate the recipient institution. Also, "In Honor Of", "To Honor the Memory Of" and "Thinking of You" cards will be mailed on request.

The Student Loan Guarantee Fund was begun in 1962. Through the year 1970, 43,631 loans were made by banks amounting to a total of $48,571,275. These were given to students, interns, and residents as follows:

Students	Interns	Residents
25,141—57.6%	6,358—14.6%	12,132—27.8%

In Connecticut 246 loans amounting to $287,100 were made during these years.

Money contributed to the Loan Guarantee Fund is held as a guarantee for repayment of loans. Each dollar in the fund puts another $12.50 to work in loans made by a commercial bank. As the loan fund increases from contributions, appreciation, and repaid loans, the money becomes available once again to guarantee still more loans.

Medical students in need of financial assistance and in full-time training can apply through the Dean of his school. The accepted applicant becomes eligible for medical education loans of up to $1500 per year—additional loans may be applied for up to a maximum of $10,000 over a seven year period.

During the year July 1, 1970 to June 30, 1971 the Woman's Auxiliary to the Connecticut State Medical Society contributed $3000 to AMA-ERF. The total contribution of the Woman's Auxiliary to the American Medical Association was $415,569.20. The national goal this year is $10 per member or about $9000 for Connecticut.

The Fiftieth Anniversary items, carefully selected by the 50th Anniversary Committee and AMA-ERF are lovely to look at and delightful to see. We know all auxiliary members will be thrilled with the items, so order now from your state chairman.

What a wonderful opportunity to make this—the Fiftieth Anniversary of the Woman's Auxiliary to the American Medical Association—the greatest ever. This is the challenge and we must get busy today and stay busy every day promoting, working and selling AMA-ERF to every auxiliary member, to doctors and to our friends.

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Topical Fluorouracil (5-FU) For Premalignant Keratoses

Fluorouracil (5-FU) is a newly marketed topical drug offered for the treatment of premalignant actinic keratoses resulting from prolonged exposure to sunlight or other sources of ultraviolet radiation, and also of premalignant keratoses associated with late X-ray dermatitis. Its use is recommended as an alternative to cryosurgery, electrodesiccation, and cold-knife surgery. Preparations of the drug recently marketed under the name Efudex (Roche) include 5% 5-FU cream and 5% and 2% 5-FU solutions in propylene glycol; Fluoroplex (Herbert Laboratories) is a 1% 5-FU solution in propylene glycol.

Clinical Effects

Topical 5-FU produces marked erythema in the area treated; the sites of keratoses usually become crusted and eroded. Healing usually takes place without scarring and with restoration of normal color and texture of the skin, but contrasting changes do occur in some patients. The drug has not proved as effective on hands and arms as on face and forehead. Topical 5-FU has produced inflammatory reactions and involution even in premalignant lesions too small to be detected clinically.

Despite some recurrences, follow-up studies have shown impressive cure rates (A. C. Williams and E. Klein, Cancer, 25:450, 1970). The removal of early lesions may prevent the development of larger and more serious keratoses and could theoretically prevent the emergence of malignant epidermal lesions. Although topical 5-FU has also been used in the treatment of some superficial basal cell carcinomas and intra-epithelial squamous cell carcinomas, the drug has not been approved for such use by the Food and Drug Administration. Surgery is the accepted treatment for these carcinomas. Actinic keratoses are to be distinguished from seborrheic keratoses or senile warts, for which 5-FU is not indicated.

Mechanism of Action

Topical administration of 5-FU inhibits DNA synthesis (W. H. Eaglstein et al., Arch. Derm., 101:132, 1970), but the mechanism of action in keratoses is not known. Immunologic reactions may play a major role in the cytolytic effect of the drug.

Dosage and Administration

In the treatment of actinic keratoses, 5-FU need not be sharply limited to areas of clinically overt involvement; for example, in the treatment of multiple keratoses involving the forehead, a thin layer of a 5-FU preparation is applied twice daily not only to the keratoses but also to the apparently normal skin between lesions. The keratoses of X-ray dermatitis may react more intensely to topical 5-FU. It should therefore be applied only once a day initially, and to small areas. Depending on the intensity of the response, the frequency of application may have to be decreased to once every two or three days or even longer.

The concentration of 5-FU to be used on a patient can be based on the severity of the involvement and the area affected, though some Medical Letter consultants begin with a weak solution and increase the concentration only if the result is not satisfactory. The scalp, forearms and hands often require the higher concentrations. The 5% solution in propylene glycol is more active than the 5% cream.

Reactions

The following reactions to 5-FU usually occur in sequence: erythema, vesiculation, erosion, ulceration, necrosis, and healing. Ulceration and necrosis may not be visible clinically. Patients should be warned of the alarming appearance and burning sensation associated with the inflammatory reaction. A course of therapy usually requires from two to four weeks for the face, longer for the extremities and trunk; it is continued until the reaction appears to have reached its height. Healing may not be complete until one to two months after therapy is stopped. If normal skin shows an excessive inflammatory response, therapy should be discontinued. Some clinicians treat small areas initially, and modify subsequent treatment if necessary.

Adverse Effects

Some absorption of topically administered 5-FU occurs and, though there are no published reports of systemic toxicity, the manufacturer cautions that thrombocytopenia has been associated with its use. The principal side effect is pain with pruritus and burning, occurring most frequently in nasolabial flexure folds and in wrinkles. The propylene glycol solutions are more irritating than cream having the same concentration. Irritation usually lessens a day or two after 5-FU is discontinued. For severe irritation, cold water compresses or topical corticosteroid preparations can be helpful. Exposure to the sun may intensify both therapeutic and irritant effects of 5-FU; it is best to warn patients against exposure. The drug occasionally causes allergic skin reactions.

Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N.Y., Vol. 13, No. 11, May 28, 1971.

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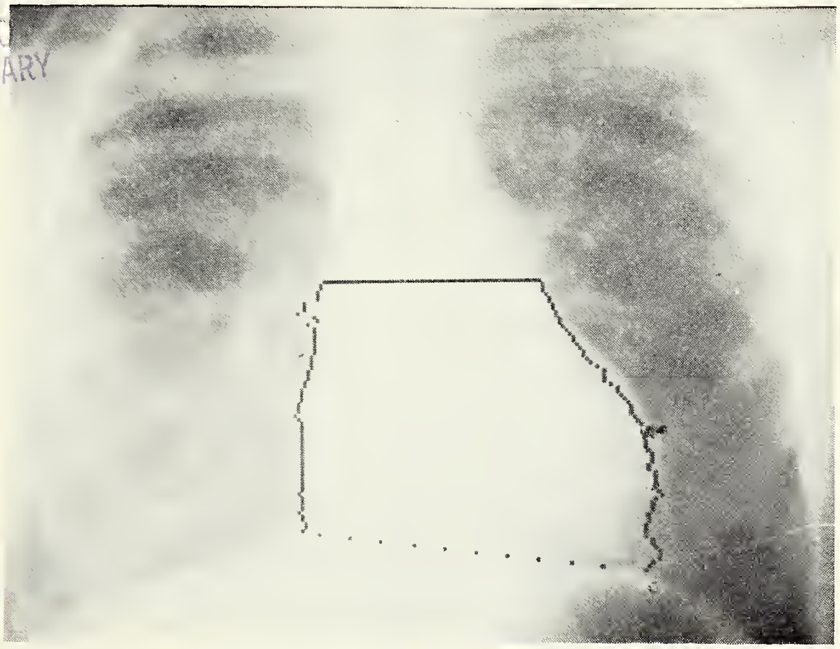

IMAGE ANALYSIS OF A RHEUMATIC HEART
Image Analysis: Application to Automated Medical Diagnosis, Allen L. Hammond, *Science, 174:* 1011-1012 (Dec. 3) 1971.
Image Analysis Laboratory, Departments of Radiology and Electrical Engineering, University of Missouri, Columbia, 1970.

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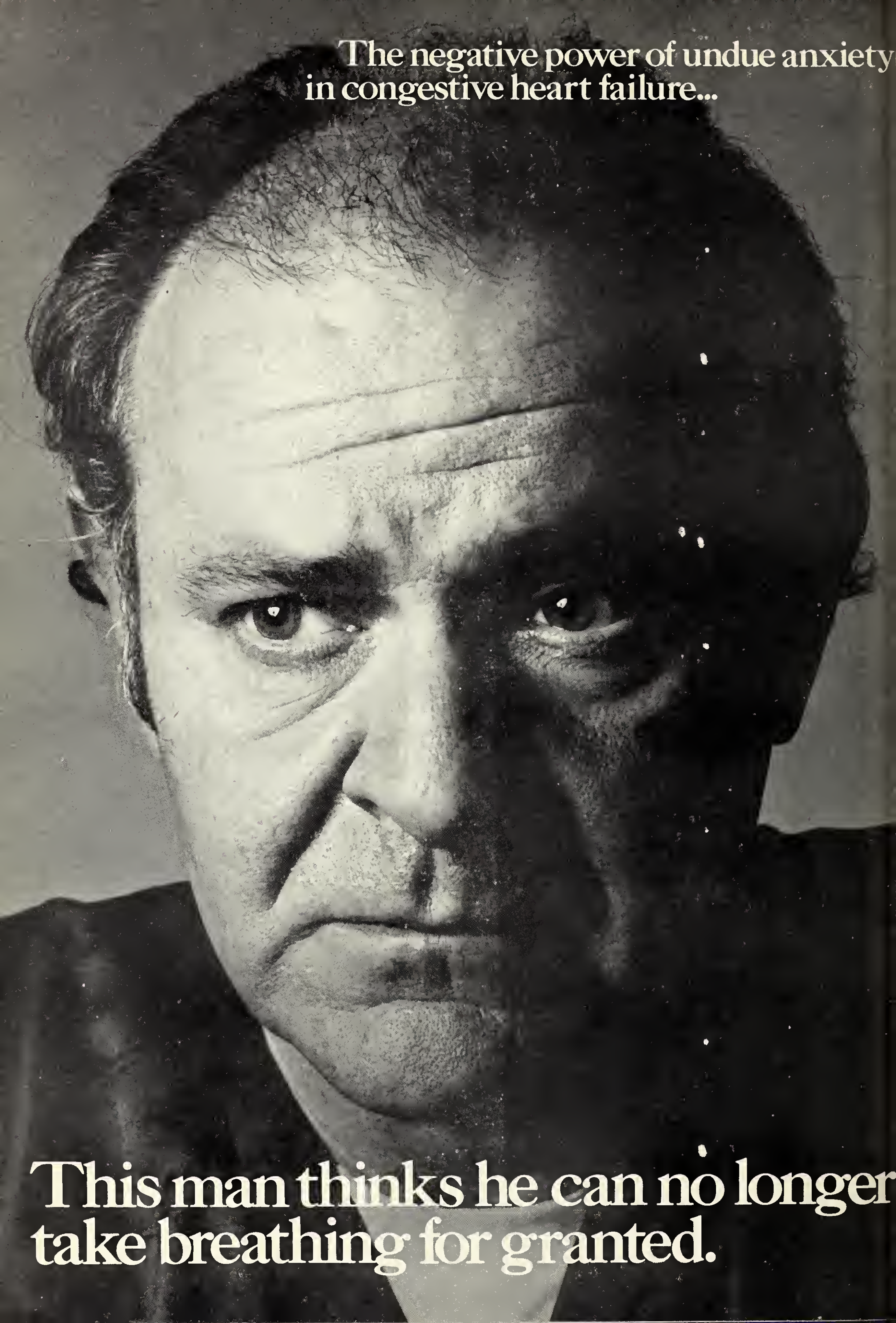
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Typical of many patients with congestive heart failure, he also suffers from severe anxiety, a psychic factor that may influence the character and degree of his symptoms, such as dyspnea. His apprehension may also deprive him of the emotional calm so important in maintenance therapy.

Aid in rehabilitation
Specific medical and environmental measures are often enhanced by the antianxiety action of adjunctive Libritabs (chlordiazepoxide). Libritabs can also facilitate treatment of the tense convalescent patient until antianxiety therapy is no longer required. Whereas in geriatrics the *usual daily dosage* is 5 mg two to four times daily, the *initial dosage* in elderly and debilitated patients should be limited to 10 mg or less per day, adjusting as needed and tolerated.

Concomitant use with primary agents
Libritabs is used concomitantly with certain specific medications of other classes of drugs, such as cardiac glycosides, diuretics, antihypertensives, vasodilators and oral anticoagulants, whenever excessive anxiety or emotional tension adversely affects the clinical condition or response to therapy. Although clinical studies have not established a cause and effect relationship, physicians should be aware that variable effects on blood coagulation have been reported very rarely in patients receiving oral anticoagulants and chlordiazepoxide HCl.

The positive power of
Libritabs®
(chlordiazepoxide)
5-mg, 10-mg, 25-mg tablets
t.i.d./q.i.d.
up to 100 mg daily
for severe anxiety accompanying congestive heart failure

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

ROCHE
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Connecticut Medicine

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Vol. 36/No. 3

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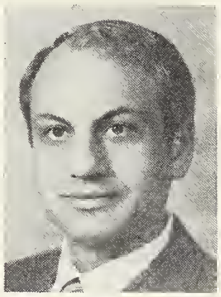
180th ANNUAL MEETING
of the
CONNECTICUT STATE MEDICAL SOCIETY
Hartford Hilton Hotel
10 Ford Street, Hartford, Connecticut

April 25, 26, 27, 1972

COMMITTEE ON PROGRAM OF THE SCIENTIFIC ASSEMBLY



DR. ESPOSITO

MICHAEL J. ESPOSITO, *Meriden, Chairman*
HOWARD LEVINE, *New Britain*
MALCOLM M. ELLISON, *New London*
WILLIAM F. ECKHARDT, JR., *New Canaan*
ROBERT L. HARRIS, *West Hartford*

MESSAGE FROM THE PRESIDENT

At this 180th Annual Meeting of the Connecticut State Medical Society there will be opportunity for every member to participate in some or all the functions listed in the published program. As President, I urge everyone to take full advantage of this excellent opportunity to benefit from his or her membership.

For those who have a special—or even a passing—interest in the ongoing business, socio-economic, legislative and scientific-educational affairs of the Society, attendance at the meeting of the House of Delegates on April 25th should prove amply rewarding. Not only can they observe their elected representatives in action but also, at the reference committee hearings during the morning session they will have a chance to express their own personal views on a variety of subjects of interest and concern to all physicians. There is only one prerequisite for participation—be among those present!

The timely theme of the two-day Scientific Assembly this year will be Clinical Pharmacology and Drug Interaction. The Program Committee is to be commended for arranging the valuable "learning panels" and outstanding formal presentations scheduled on April 26 and 27, all of which are related to the central theme and, collectively, cover a sufficiently wide range of medical entities to satisfy both general and special tastes. The importance of continuing medical education for physicians is much in the news lately and this fine opportunity to increase our knowledge should not be passed up by any of us for less than compelling reasons.

On the more social side, there are several functions that merit our attention. As in recent years, there will be an exhibit of works of art produced by member physicians and their families which is sponsored by the Connecticut Physicians' Art Association. At the Delegates' luncheon on the 25th, the members and guests of the House will be privileged to hear an address by Dr. Russell B. Roth, Speaker of the House of Delegates of the American Medical Association and candidate for the office of AMA President-Elect. Unfortunately due to the limitation of facilities, attendance at the luncheon must be restricted to the membership of the House. However, on the evening of April 26 the Annual Dinner of the Society for all members will be held, preceded by a social hour. Featured at the dinner will be the inauguration and inaugural address of the incoming President of the Society and the presentation of certificates and pins to a new group of 50 Year Members. The dinner is always a pleasant occasion and offers physicians and their spouses a few hours of relaxation in which to renew old acquaintances and, more than likely make some new ones.

I trust that by now I have whetted your appetite to share with me the benefits and responsibilities of membership at this 180th Annual Meeting, and I will look forward to seeing you there.

FREDERICK C. WEBER, JR.

GENERAL INFORMATION — READ CAREFULLY

REGISTRATION

The registration desk will be located on the mezzanine floor and everyone attending the meeting is requested to register. There will be no charge for registration and all members of the Society will be given a guest luncheon ticket when and only if they register.

PARKING

There are ample parking facilities at the hotel and in the surrounding area. If you wish, you may drive up to the door of the hotel and an attendant will park your car for you.

TELEPHONE

Telephone messages will be received at Hartford 249-5611.

LUNCHEONS

Luncheons will be served in the Cities Rooms on the Mezzanine, on April 26 and April 27 and ALL MEMBERS OF THE SOCIETY REGISTERING WILL BE THE GUEST OF THE SOCIETY. PLEASE REMEMBER A LUNCHEON TICKET WILL BE GIVEN TO MEMBERS ONLY IF THEY REGISTER.

HOTEL ACCOMMODATIONS

Persons who wish to remain overnight should make reservations not later than two weeks prior to opening date of the meeting. Reservations will be held until 6:00 P.M. on the day of arrival, unless later hour is specified. Please indicate in your letter that you are attending the Connecticut State Medical Society meeting. Your letter should be directed to the Front Office Manager, Hartford Hilton Hotel, 10 Ford Street, Hartford, Connecticut.

ANNUAL DINNER

The Annual Dinner will be held at the hotel on Wednesday, April 26, 1972. The social hour will be at 6:15 P.M. and the dinner at 7:00 P.M. All persons attending the dinner will be the guests of the Society at the social hour which will begin *promptly* at 6:15 P.M. and end *promptly* at 7:00 P.M. Your reservation for dinner should be sent in as soon as possible.

PROGRAM

General scientific sessions will be held on Wednesday and Thursday in the Terrace Room and Section meetings will be held in the rooms listed in the program. "Round Table Discussions" will again be held on Wednesday and Thursday mornings.

EXHIBITS

All the exhibits will be located in the ballroom. Physicians should take advantage of the opportunity to review "under one roof" what is new and timely by visiting the commercial and educational exhibits.

ROUND TABLE DISCUSSIONS

Members of the Society are invited and encouraged to participate in the new learning technique; Round Table Discussions, or "Learning Panels". Four of these panels will be held on Wednesday, April 26 and four on Thursday, April 27. The subject, time and place for each is published in the Program that follows. The respective "Learning Panels" will be chaired by experienced physicians who will lead their groups, of not more than 15 participants, through in-depth examination of the topics assigned. Active participation in the group discussion will be limited to members who have pre-registered. Registration forms will be mailed to members with the Program of the meeting. Members, who have not pre-registered, will be welcome to attend the panels as observers only, within the limits of available seating capacity.

ANNUAL MEETING OF THE HOUSE OF DELEGATES

Tuesday, April 25

Terrace Room Mezzanine

Presiding: KENNETH F. BRANDON, *Hartford, Speaker of the House*
TIMOTHY F. NOLAN, *Greenwich, Vice-Speaker of the House*

7:30 REGISTRATION OF DELEGATES
Continental Breakfast for Delegates and Official Guests
8:30 CALL TO ORDER
OPENING SESSION
REFERENCE COMMITTEE HEARINGS
1:15 LUNCHEON—Cities Rooms—Mezzanine
Guest Speaker: RUSSELL B. ROTH, M.D. Speaker, AMA House of Delegates
3:00 CALL TO ORDER—Terrace Room
FINAL SESSION
6:30 ADJOURNMENT
Reception and Dinner for Delegates and Official Guests—Cities Rooms—Mezzanine

SCIENTIFIC PROGRAMS

Wednesday, April 26

MORNING SESSIONS

8:30 REGISTRATION—Mezzanine

ROUND TABLE DISCUSSIONS

8:45-10:00 Fourth Floor in Rooms Designated

PHARMACOLOGICAL PROBLEMS OF THE PREGNANT STATE—Room 412
Group Leader: JACK N. BLECHNER, *New Briitain, Connecticut*

LABORATORY PROBLEMS RESULTING FROM THE USE OF COMMON DRUGS—Room 416
Group Leader: JAMES E. O'BRIEN, *Hartford, Connecticut*

PHARMACOLOGICAL CONSIDERATIONS IN RENAL DISEASE—Room 420
Group Leader: GEORGE F. THORNTON, *Waterbury, Connecticut*

PHARMACOLOGICAL PROBLEMS OF ANTI-ARRYTHMIC DRUGS—Room 424
Group Leader: MARTIN J. KRAUTHAMER, *Darien, Connecticut*

10:00 INTERMISSION TO VISIT EXHIBITS

TERRACE ROOM

10:25 OPENING REMARKS
MICHAEL J. ESPOSITO, *Meriden, Connecticut, Chairman, CSMS Committee on Program of Scientific Assembly*

SYMPOSIUM ON THE NEW CLINICAL PHARMACOLOGY

Presiding: ROBERT J. LEVINE, *New Haven, Connecticut*

10:30 WHAT YOU NEED TO KNOW—BASIC CONCEPTS
BERT N. LA DU, *New York City; Professor and Chairman, Department of Pharmacology; Visiting Pediatrician, Bellevue Hospital and University Hospital*

11:15 PRACTICAL ASPECTS OF DRUG INTERACTIONS
JAN KOCH-WESER, *Boston, Massachusetts; Associate Professor of Pharmacology, Harvard Medical School; Chief of Clinical Pharmacology Unit, Massachusetts General Hospital*

12:00 PANEL DISCUSSION
Moderator: WILLIAM F. ECKHARDT, JR., *New Canaan, Connecticut*
Panelists: BERT N. LA DU, JAN KOCH-WESER, ROBERT J. LEVINE

12:30 INTERMISSION TO VISIT EXHIBITS

1:00 LUNCHEON—*Cities Rooms*

AFTERNOON SESSION

TERRACE ROOM

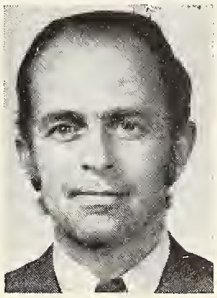
Presiding: JAMES E. O'BRIEN, *Hartford, Connecticut*

2:00 CLINICAL PHARMACOLOGY AND PROBLEMS CREATED BY NEWER DIURETIC DRUGS
PAUL J. CANNON, *New York City; Associate Professor of Medicine, College of Physicians and Surgeons, Columbia University; Associate Attending Physician, Columbia-Presbyterian Medical Center*

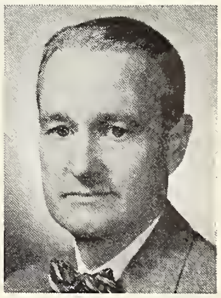
2:45 CURRENT THERAPY OF HYPERTENSION
ROBERT W. WILKINS, *Boston, Massachusetts; Wade Professor of Medicine, Boston University School of Medicine; Physician-in-Chief, University Hospital*

3:30 INTERMISSION TO VISIT EXHIBITS

BERT N. LADU
New York, New York



JAN KOCH-WESER
Boston, Massachusetts



ROBERT W. WILKINS
Boston, Massachusetts

Wednesday, April 26

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON DERMATOLOGY

2:30 Room 424

President: Ralph L. Parker, *Bridgeport*
Secretary: Thomas P. Kugelman, *Hartford*

Immunoglobulin E

William E. Clendenning, *Hanover, New Hampshire; Chairman, Section of Dermatology, Hitchcock Clinic*

JOINT MEETING

SECTION ON INTERNAL MEDICINE

President: Kenneth R. Knox, *Hartford*
Secretary: James W. Innes, *Greenwich*

CONNECTICUT DIABETES ASSOCIATION

3:30 Rooms 408-412

President: Neil Auerbach, *Norwalk*
Secretary: James C. Hart, *Hartford*

Long Term Treatment of Adult Diabetes Mellitus

Charles M. Clark, *Indianapolis, Indiana; Clinical Investigator, Veterans Administration Hospital and Assistant Professor of Medicine, Indiana University School of Medicine*

SECTION ON NEUROLOGY

3:30 Boston Room

President: Gustav W. Anderson, *Hartford*
Secretary: J. William Healy, *Hartford*

The Significance of Serum Anti-Convulsant Determination in the Control of Epilepsy

Brian Gallagher, *New Haven, Connecticut; Associate Professor of Neurology, Yale University School of Medicine*

SECTION ON OBSTETRICS AND GYNECOLOGY

3:30 Room 420

President: Philip C. Dennen, *Waterbury*
Secretary: Peter A. Goodhue, *Stamford*

Prostaglandins and Reproduction

Leon Speroff, *New Haven, Connecticut; Assistant Professor of Obstetrics and Gynecology, Yale University School of Medicine*

SECTION ON ORTHOPEDICS

4:00

Hunt Memorial Building
230 Scarborough Street, Hartford
President: James F. Donovan, *Hartford*
Secretary: Martin L. Karno, *New London*

Fractures of the Hip

William K. Massie, *Lexington, Kentucky, Orthopedic Surgeon*

Wednesday, April 26

SECTION ON PATHOLOGY

3:30 Room 404

President: Hollis N. Truax, *Norwalk*
Secretary: Daniel W. Benninghoff, *Greenwich*

Hemolytic Anemia

Leon W. Hoyer, *Farmington, Connecticut; Associate Professor of Medicine, University of Connecticut Health Center*

SECTION ON PROCTOLOGY

3:30 Buffalo Room

President: Bernard J. Kaplan, *Hartford*
Secretary: Sanford Savin, *Bridgeport*

Business Meeting

Election of Officers

Discussion of Unusual Cases

SECTION ON RADIOLOGY

3:30 New York-Washington Rooms

President: John H. Woodruff, *Hartford*
Secretary: Carl W. Scheer, *Meriden*

Percutaneous Transhepatic Cholangiography

Robert B. Toffler, *New Haven, Connecticut; Assistant Professor of Radiology, Yale University School of Medicine*

SECTION ON UROLOGY

3:30 Room 416

President: Elwood F. Ireland, Jr., *Bridgeport*
Secretary: James P. Roach, *Bridgeport*

Renal Transplantation

Martin Schiff, Jr., *New Haven, Connecticut; Assistant Professor of Urology, Yale University School of Medicine*

CONNECTICUT ASSOCIATION OF MEDICAL EXAMINERS

12:30 Rooms 436-440

President: Samuel B. Rentsch, Sr., *Derby*
Secretary: Joseph E. Daly, *Waterbury*

12:30 Luncheon for Medical Examiners, Coroners and Guests (Dutch Treat)

Guest Speaker: Elliott M. Gross, *Hartford, Connecticut; Chief Medical Examiner, State of Connecticut*

Subject: Investigation of Sudden and Unexpected Deaths Under the Medical Examiners System in the State of Connecticut

Business Meeting to Follow

Election of Officers

Wednesday, April 26

WOMAN'S AUXILIARY TO THE CONNECTICUT STATE MEDICAL SOCIETY

TWENTY-EIGHTH ANNUAL MEETING

HARTFORD HILTON HOTEL

The Club Room—Fourth Floor

President: Mrs. Forrest Gibson, *Farmington*
Recording Secretary: Mrs. Otto M. Hirschfeld, *West Hartford*
Corresponding Secretary: Mrs. Gerard V. Levreault, *Newington*

10:00 Registration

10:30 Business Meeting

1:00 Social Hour and Luncheon

Guest Speaker: Mrs. Howard Liljestrand, *Director, Woman's Auxiliary of the American Medical Association, Chairman of International Health Activities*

Induction of Officers for 1972

Presentation of President's Pin

ANNUAL DINNER OF THE SOCIETY

HARTFORD HILTON HOTEL

10 Ford Street, Hartford

Social Hour 6:15 P.M. Dinner 7:00 P.M.

PROGRAM

Presiding: Frederick C. Weber, Jr., *Greenwich*

Presentation of Guests and Delegates from State Medical Societies

Fifty Year Membership Awards

Freeman Pell Clason, *West Hartford*
Maurice M. Hillman, *New Haven*
Wilmarth Bradford Walker, *Cornwall*
William Witter Wright, *West Hartford*
Isidore Hendel, *New London*
Luther Kyner Musselman, *Old Lyme*
Winfield Emmons Wight, *Thomaston*

Inauguration of Incoming President

David Arthur Grendon, *Sharon*

President's Address

Dinner Music

Thursday, April 27

MORNING SESSIONS

8:30 Registration—Mezzanine

ROUND TABLE DISCUSSIONS

8:45-10:00 Fourth Floor in Rooms Designated

Pharmacological Problems of the Newborn—Room 412
Group Leader: Robert L. Harris, *West Hartford, Connecticut*

Pharmacological Problems of Drug Abuse—Room 416
Group Leader: Robert A. Kramer, *Hartford, Connecticut*

Clinical Pharmacology of the Common Anti-Neoplastic Drugs—Room 420
Group Leader: Ronald C. DeConti, *New Haven, Connecticut*

Current Status of Oral Hypoglycemic Agents—Room 424
Group Leader: Philip Felig, *New Haven, Connecticut*

10:00 Intermission to Visit Exhibits

TERRACE ROOM

SYMPOSIUM ON THE RHEUMATOID STATE

Presiding: Naomi Rothfield, *Hartford, Connecticut*

10:30 What's Wrong in Rheumatic Disease—Basic Mechanisms

Gerald Weissmann, *New York City; Professor of Medicine, New York University School of Medicine; Attending Physician, Bellevue Hospital*

11:15 Anti-Inflammatory Drugs—Clinical Usage

Thomas G. Kantor, *New York City; Associate Professor of Clinical Medicine, New York University Medical Center; Associate Attending Physician, University Hospital; Chief, Section of Clinical Pharmacology, Department of Medicine, New York University Medical Center*

12:00 Panel Discussion

Moderator: Howard Levine, *New Britain, Connecticut*
Panelists: Gerald Weissmann, Thomas G. Kantor, Naomi Rothfield

12:30 Intermission to Visit Exhibits

1:00 Luncheon—Cities Rooms

AFTERNOON SESSION

TERRACE ROOM

PROGRAM ARRANGED WITH CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

Presiding: Harry J. Tamoney, Jr., *Hartford*

2:00 Patho-Physiology and Dissolution of Gall Stones

Johnson L. Thistle, *Rochester, Minnesota; Instructor in Medicine, Mayo Graduate School; Consultant in Internal Medicine and Gastroenterology, Mayo Clinic*

2:45 Surgical Implications of Gall Stones and Their Dissolution

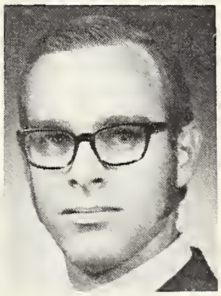
Charles K. McSherry, *New York City; Associate Professor of Surgery, Cornell University Medical College; Associate Attending Surgeon, New York Hospital*

3:30 Discussion—Questions and Answers

Intermission to Visit Exhibits

Gerald Weissman
New York, New York

Thomas G. Kantor
New York, New York



Johnson Thistle
Rochester, Minnesota

Charles M. McSherry
New York, New York

Thursday, April 27

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON ALLERGY

3:30 Room 404

President: George A. Sprecace, *New London*
Secretary: Philip I. Weisinger, *New Haven*

Report of Section Ad Hoc Committee on Peer Review
General Discussion

SECTION ON ANESTHESIA

3:30

Hunt Memorial Building
230 Scarborough Street, Hartford

President: Aaron Bobrow, *Hartford*
Secretary: Henry T. Bonney, *Hartford*

THE FIFTH RALPH M. TOVELL MEMORIAL LECTURE

Anesthesia and the Coronary Patient
Arthur Stanley Keats, *Waco, Texas; Professor and Chairman, Department of Anesthesiology, Baylor University College of Medicine*

SECTION ON GASTROENTEROLOGY

3:30 Room 408

President: Saul S. Milles, *New Haven*
Secretary: Robert S. Rosson, *Hartford*

2:00 Members of the Section on Gastroenterology are invited to attend the program arranged by the Connecticut Society of American Board Surgeons in the Terrace Room on the subject of gall stones.

4:00 Disorders of Esophageal Bolus Transport—Room 408
Daniel Winship, *Columbia, Missouri, Associate Professor of Medicine, University of Missouri School of Medicine*

SECTION ON GENERAL PRACTICE

3:30 Room 424

President: John C. Wright, *Manchester*
Secretary: Joseph C. Czarsty, *Oakville*

New Trends in Family Practice Education
Speaker to be announced
Election of Officers

SECTION ON NEUROSURGERY

3:30 Room 436

President: Lycurgus M. Davey, *New Haven*
Secretary: Donald W. Cooper, *New London*

Symposium on the Problem of Back Pain

Study of Motion in the Lumbo-Sacral Spine. A Computer Model.
William J. German, *New Haven, Connecticut; Professor Emeritus of Neurosurgery, Yale University School of Medicine*

Back Pain. Prelude to Lumbar Disc Syndrome?
Lycurgus M. Davey, *New Haven, Connecticut; Associate Clinical Professor of Neurosurgery, Yale University School of Medicine*

Discussants: David C. Cavicke, *New London*; James C. Collias, *Hartford;* Francis H. O'Brien, *Waterbury*

Neurosurgical Progress at the University of Connecticut Medical School
Melville P. Roberts, Jr., *Farmington, Connecticut; Professor of Neurosurgery, University of Connecticut Medical School*

SECTION ON OPHTHALMOLOGY

3:30 The Club Room

President: Daniel M. Taylor, *New Britain*
Secretary: David W. Parke, *Meriden*

Recent Advances in Ophthalmic Microsurgery
Richard C. Troutman, *New York City; Professor of Ophthalmology, State University of New York Medical Center (Downstate), Brooklyn, New York*

SECTION ON PHYSICAL MEDICINE

3:30 Rooms 416-420
President: Sung J. Liao, *Middlebury*
Secretary: Karen Shanazarian, *Waterbury*

The History of Acupuncture
Frederick Kao, *New York City; Professor of Physiology, State University of New York Medical Center (Downstate), Brooklyn, New York*

The Application and Technique of Acupuncture
Sung J. Liao, *Middlebury, Connecticut; Associate Clinical Professor, Rehabilitation Medicine, Boston University School of Medicine*

CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

Terrace Room
President: William A. Whalen, *Willimantic*
Secretary: James H. Foster, *Hartford*

2:00 See General Program—Thursday 2:00 P.M.
4:00 Connecticut Society of American Board Surgeons' Survey on Abdominal Trauma
Gerald O. Strauch, *Stamford, Connecticut, Surgeon*
5:00 Social Hour
6:00 Dinner—Guest Speaker: Peter Goldmark, *Ph.D., Stamford, Connecticut, Former Director of CBS Laboratories*
Subject: Medicine in the New Rural Society

TECHNICAL EXHIBITS

Aetna Life and Casualty, Hartford, Connecticut
Biochemical Procedures, Hillside, New Jersey
(an affiliate of Mead Johnson Co.)
Coca-Cola Company, USA
Dictaphone Corporation, Hartford, Connecticut
Arthur W. Eade Insurance Agency, Hamden, Connecticut
Fiduciary Capital Corp., New York, New York
Group Insurers, Inc., New Haven, Connecticut
Hoechst Pharmaceutical Company, Somerville, New Jersey
Ives Laboratories, New York, New York
Eli Lilly & Company, Indianapolis, Indiana
Marion Laboratories, Inc., Kansas City, Missouri
Mead Johnson Laboratories, Evansville, Indiana
Medical Personnel Pool, Hartford, Connecticut
Merck Sharp & Dohme, West Point, Pennsylvania
Parke, Davis & Company, Detroit, Michigan
Crowley & Gardner/Surgeons & Physicians, Inc., Boston, Massachusetts
Trans-American Collections, Inc., Norwalk, Connecticut
Uxbridge Professional Services, Inc., Stamford, Connecticut

EDUCATIONAL EXHIBITS

Prevention of Lead Paint Poisoning—
Connecticut State Department of Health
Connecticut Tumor Registry
Connecticut State Department of Health
Prevention of Blindness in Action—Glaucoma Testing
Connecticut Society for the Prevention of Blindness
Section on Ophthalmology, Connecticut State Medical Society
Student Research at the University School of Medicine
University of Connecticut School of Medicine
Industrial Medical Association: Its Objectives, Activities, and Services
Connecticut Industrial Medical Association
Nutrition Educational Resources
Connecticut Dairy and Food Council, Inc.
AMA-ERF Exhibit
Woman's Auxiliary to the Connecticut State Medical Society
COMPAC Educational Exhibit

ART EXHIBIT

Connecticut Physicians' Art Association

SPECIAL NOTICE

Hospital residents, interns and medical students are cordially invited to attend this meeting.

Members of the Connecticut State Pharmaceutical Association and the Connecticut Hospital Pharmacists' Association are also invited to attend this meeting.

Artists — Attention!

GENERAL INFORMATION: The Connecticut Physicians' Art Association is planning the 1972 Art Exhibit in conjunction with the annual meeting of the Conecticut State Medical Society. The following is submitted for guidance to art hobbyists.

WHERE: Hartford Hilton Hotel, Hartford, Connecticut
WHEN: April 25, 26, 27, 1972

ELIGIBILITY: Physicians (members of the Connecticut State Medical Society) and their families are cordially invited to join this group of art hobbyists. (In the case of children and other members of physician's family, kindly indicate relationship to sponsor.) All previous exhibitors are invited to show their works at this meeting, and new exhibitors are welcomed. Works eligible will include oil, water colors, tempora, black and white etchings, photography, pastels, collages, mixed media and sculpture. Paintings over 24 × 30 will be hung only at the discretion of the art committee depending upon available space.

JUDGING: Art works will be judged in four categories: 1. Children under 16 years (children over 16 will be judged with adults); 2. beginners; 3. intermediates; 4. professionals. Pictures should be framed and wired for hanging. The exhibit will be judged by professional artists.

COST: A hanging fee of two dollars ($2.00) will be charged for each entry and fifty cents (50¢) for children under 16 years with two entries per artist. (Space requirements have caused our limiting the entries to two this year, as just noted.)

HOW TO APPLY: Entry blanks will be mailed to former exhibitors and also may be obtained by writing to the addresses of the committee listed below. One half of the enry blank should be submitted to me at the below address with your check prior to April 14, 1972. The other half should be attached to the picture. Make checks payable to the Conecticut Physicians' Art Association. Please fill in entry blanks completely so that the entry can be categorized early in the above noted four categories.

SUBMITTING: Art works must be submitted to a representative of the Art Association in the lobby of the Hartford Hilton Hotel on Sunday, April 23, 1972, between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. It may be possible to aid exhibitors with the transportation of art works by contacting members of the committee noted below. These art works must be picked up on Thursday, April 27, 1972, between 12 and 4 P.M. Members of the art committee or their representatives will be in attendance at the display throughout the exhibit at the state meeting. The Connecticut State Medical Society, the hotel (nor the Art Association) can assume no responsibility for loss or damage of any cause to art work.

Under no condition can art work be accepted after April 14th.

If further information is needed, the following persons may be contacted:

Eugene Rightmyer, M.D., President, 114 Sherman Avenue, New Haven; Mrs. Orvan Hess, Vice President, 29 Old Orchard Road, North Haven; Mrs. Albin Anderson, Chairman, Woman's Auxiliary, 17 Drury Lane, West Hartford; Mrs. Lowell Olson, Co-Chairman, Woman's Auxiliary, 85 River Road, North Haven; Ann Murphy, 8 E. Normandy Drive, West Hartford; Mrs. John Shoukimas, 26 Pheasant Hill Drive, West Hartford; Edward Williams, M.D., 580 Hillside Avenue, Naugatuck; Herman Austrian, M.D., 935 White Plains Road, Trumbull; Kurt Oster, M.D., 880 Lafayette Boulevard, Bridgeport; Stewart J. Petrie, M.D., 56 Minerva Street, Derby; Mrs. Mark Hayes, 163 Ridgewood Avenue, North Haven; Mrs. Clifford Wilson, 19 East Town Street, Norwich; Mrs. Sidney Hurwitz, 35 Williamsburg Drive, Woodbridge; Mrs. A. vonGraevenitz, 2064 Chapel Street, New Haven; Mrs. Allen Silberstein, 51 Prospect Street, Portland; Mrs. Robert Bowen, High Street, South Coventry, and Mrs. R. Gilman, 3 Willowbrook Road, Storrs.

Eugene Rightmyer, M.D., *President*
Connecticut Physicians' Art Association

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Adverse Reactions: *Central Nervous System:* Drowsiness, ataxia, dizziness, slurred speech, headache, vertigo, weakness, paresthesias, impairment of visual accommodation, euphoria, overstimulation, paradoxical excitement, fast EEG activity. *Gastrointestinal:* Nausea, vomiting, diarrhea. *Cardiovascular:* Palpitations, tachycardia, various forms of arrhythmia, transient ECG changes, syncope; also, hypotensive crises (including one fatal case). *Allergic or Idiosyncratic:* Usually after 1-4 doses. Milder reactions: itchy, urticarial, or erythematous maculopapular rash (generalized or confined to groin). Others: leukopenia, acute nonthrombocytopenic purpura, petechiae, ecchymoses, eosinophilia, peripheral edema, adenopathy, fever, fixed drug eruption with cross reaction to carisoprodol, and cross sensitivity between meprobamate/mebutamate and meprobamate/carbromal. More severe, rare hypersensitivity: hyperpyrexia, chills, angioneurotic edema, bronchospasm, oliguria, anuria, anaphylaxis, erythema multiforme, exfoliative dermatitis, stomatitis, proctitis, Stevens-Johnson syndrome; bullous dermatitis (one fatal case after meprobamate plus prednisolone). Stop drug, treat symptomatically (e.g., possible use of epinephrine, antihistamines, and in severe cases corticosteroids). *Hematologic:* Agranulocytosis and aplastic anemia (rarely fatal), but no causal relationship established. Rarely, thrombocytopenic purpura. *Other:* Exacerbation of porphyric symptoms.
Usual Adult Dosage: 1200 to 1600 mg daily, in three or four divided doses; doses above 2400 mg daily not recommended.
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PRESIDENT'S PAGE

The Health Maintenance Organization (H.M.O.) is receiving increasing publicity again as a method of providing and paying for health care. It is being promoted largely on the basis of its ability to prevent sickness. How does the H.M.O. prevent an illness? By "maintaining health" obviously, hence the name.

If we examine how the public is maintaining its health at the present time, we find that the preventive vaccines and vitamins are thoroughly known to the practicing physician and he is the agent who promotes their effective use.

The next step in prevention is in early diagnosis of disease by periodic examinations, routine chest X-rays, and Pap smears. These methods are also well known, and practiced frequently. Some patients find this method attractive and co-operate fully in regular check ups. Many do not and, therefore add to the number of cases seen in more serious stages of illness. Their failure to enter the health care system at an early stage is not to be blamed on the medical profession, the local health agencies, hospitals, or even the advertising or news media, all of whom have promoted the check up concept in one way or another.

We now come to consider the vast majority of patients who despite prevention and early detection acquire a major illness. These are mostly the older patients who are afflicted with vascular disease of one sort or another (heart disease or stroke), or cancer. Once afflicted this group provides for the majority of patients requiring long term hospital care. They are absolutely dependent on hospital insurance, private or government. These patients get well slowly or remain invalids and the expense of their care becomes a tragic burden for the family.

Health Maintenance Organizations do not have any more answers for these patients than Foundations or the private practitioner. It is on these cases that Medicare funds are being spent in largest amounts; and on these patients in hospitals and extended care facilities that the benefits promised are being reduced most drastically and surreptitiously. The government must take this large group of patients into account financially. HEW surely knows the facts on the numbers and expenses of these individuals. Their expenses can be budgeted and they should be told if their benefits are to be cut, rather than find they must pay for a part of an expensive illness. The promotion of medical utopia through H.M.O.'s must be shown to be unable to prevent long term illness and invalidism. The medical profession is the only group capable of seeing this in proper perspective and of bringing it to the attention of the public.

Frederick C. Weber, Jr., M.D.

Prevention of Child Abuse: Current Progress in Connecticut:

I. "The Problem"

John B. G. Trouern-Trend, M.D. and Martha Leonard, M.D.

This is the first of a series of articles whose purpose is to review Child Abuse from the physician's standpoint, to outline the legal aspects and describe the efforts of the Commissioner of Health's Advisory Committee on Child Abuse in working towards new legislation, and to discuss this legislation, (effective October 1, 1971,) in detail.

The term "battered child syndrome" used first by Kempe,[1] et al, served the important purpose of focusing professional and public attention on this extreme manifestation of disordered mothering behavior. Unfortunately, this emphasis on *severe* physical injury tends to obscure the fact that this is the end of a wide spectrum; it is only the "top of the iceberg." As we turn more towards a "preventive" approach in seeking the enhancement of normal development, it becomes unacceptable to wait for major physical battering to occur before we recognize a problem and attempt to intervene. The use of the term "child abuse" has broader implications appropriate to these problems.

There has been much argument as to the size of the problem. Some rely on the numbers of cases of child abuse reported in the various states as a result of reporting legislation enacted during the early and mid '60s. In such a nation-wide survey, Gil[2] found that 5,993 cases of abuse were reported through local channels in 1967. This figure represents an incidence rate of about 7.5 per 100,000 children per year. In Connecticut, 102 cases were reported from October 1, 1967 to August 31, 1968, at 11.5 per 100,000 children per year while the most recent figure, 378 from July 1, 1970 to June 30, 1971, (see table 1), represents an incidence of 37.8 per 100,000 children per year. However, those who are directly involved in handling cases or suspected cases of abuse are well aware that for various reasons many possible reports never get made. Gil points out that, "since abuse incidents tend to occur in the privacy of a family's home, not all of them come to the attention of individuals or institutions required to report, and not all incidents that are known to such persons are actually reported." Intensive studies of small groups suggest a much higher overall incidence than that based on national reporting figures. Holter & Friedman[3] in two week surveys of *all* children under 6 years seen in an emergency room in Rochester, New York for accidents, found that about 10% had injuries "due to maltreatment." Stone[4] found that 8% of children with burns admitted to Cook County Hospital in Chicago were abused or suspected of having been abused: the mortality in that group was 20%.

Failure to consider the possibility of abuse is one of the principle causes of under-reporting. This lack of awareness is particularly regrettable in

TABLE 1

The cases of suspected child abuse reported in Connecticut between 7-1-70 and 6-30-71 totaled 378 (181 male and 197 female): their *age distribution* was as follows:

Less than 1 year	60
1-3 years	68
3-13 years	187
13-18 years	63
Types of Abuse:	
"Beatings"	244
Malnutrition and Failure to Thrive	39
Burns	38
Sexual Molestation	27
Fractures (excluding skull)	20
Fractures of Skull	12
Poisonings	6
Concussion	5
Incest and Rape	5
Internal Injuries (excluding brain)	3
Subdural Hematoma	3
Death	9
Miscellaneous	17

DR. JOHN B. G. TROUERN-TREND, Assistant Professor of Pediatrics, University of Connecticut Health Center, Hartford, Connecticut.

DR. MARTHA LEONARD, Associate Professor of Clinical Pediatrics, Child Study Center, Department of Pediatrics, Yale University, New Haven, Connecticut.

Emergency Rooms where substantial numbers of children are treated for accidents and injuries. A history which is inadequate to explain the injuries, conflicting histories from parent or guardian, a history "explaining" several lesions of different ages by one episode, an unexplained delay in seeking medical assistance: all of these should make the physician concerned about possible abuse. A history of repeated injuries should also raise the question. Unfortunately, this may not be revealed by the parent or the child's previous medical record since he may have been treated for prior episodes at different medical care facilities.

Certain *types* of injury should arouse suspicion, especially abrasions, bruises, contusions and burns in younger children. Sussman[5] lists the following characteristics of skin lesions possibly resulting from abuse: 1) the lesions are often concentrated in clusters on the trunk, buttocks, head, and proximal segments of extremities; 2) the lesions are the same shape as the instrument used to inflict them, i.e., straight, curvilinear, circular or jagged; 3) bleeding into the skin is purpuric, almost never petechial; 4) skin lesions are often of different ages. X-ray evidence of repeated fractures is unlikely to point to any cause other than abuse—except perhaps in osteogenesis imperfecta. Infantile cortical hyperostosis and scurvy may produce radiographic appearances that might raise suspicion of abuse.

From the various surveys, it is becoming apparent that there are high-risk factors, awareness of which may be of great help to the physician or other health professional faced with the decision as to whether or not the question of child abuse should be pursued in a given case. Any major emotional, social, or financial stresses, or serious illness within the family may contribute towards child abuse. At particular risk is the socially isolated family with "no one to talk to." The parents who emphasize their child's "irritability" or "frequent crying" are more likely to be abusers. At risk also is the child singled out by the parent as "different" and "bad." A history of the parent having been abused or treated harshly during their own childhood seems to be associated with a greater likelihood of their abusing their offspring: violence breeds violence!

The lack of alertness to this type of problem or even positive reluctance on the part of many physicians to consider the possibility of abuse has many contributing factors. The simplest is that of not thinking of the possibility. Unfortunately, our systems of emergency care tend to focus so narrowly on the presenting injury that the episode tends not to be considered in full context except in such severe cases that non-accidental injury is obvious at a glance. Fragmented, uncoordinated care tends to obscure recurring patterns of injuries. Many physicians find it emotionally difficult to conceive of the possibility that a concerned, affectionate parent could have abused their child. It is then easier for the physician to deal with his feelings by ignoring the clues which should have led to further investigation.

There seems to be widespread misunderstanding about the fact that for a report to be required, there must be "reasonable grounds to suspect" abuse not "*proof* beyond reasonable doubt"—which is frequently unobtainable. Many of those who are required to report are unaware of the legal immunity granted those who "report in good faith." Physicians who have a long and close relationship with their patients, may be deterred by the possible social and/or financial repercussions of reporting a suspicion of abuse. A major reason for reluctance to report has been physicians' fear that a report will result in a *punitive* rather than therapeutic intervention.

The following case illustrates many of the above mentioned points.

Case Report

A 2½ year-old boy was brought by his mother to the Emergency Room with a history of inability to walk for 12 to 24 hours prior to admission after "falling down from bed." There had been no loss of consciousness and no change in his speech.

Developmental milestones were reported as "normal," and there was no history of repeated hospital visits for trauma. He had two brothers—aged 6 years and 6 months—all three children being by different fathers. The patient's father lived in another city, while the other fathers were in jail for use of narcotics. The family was supported by State Welfare. The mother reported that the eldest child constantly hit the patient and the mother's sister did likewise when babysitting. The other two children showed no physical abnormalities on examination.

On physical examination, his vital signs were within normal limits; he was conscious, but appeared "withdrawn." His height was at the 10th percentile and weight at the 3rd percentile. The positive findings were confined to the skin and nervous system. He had multiple healed scars of various sizes, including scratch marks and teeth marks. An open 1cm wound was present on the forehead and two hematomas were observed over the left temporal area. There were fresh contusions over the legs. He was unable to sit or stand but the remainder of the neurological findings were confined to the *right side*: minimal facial weakness; absence of voluntary or spontaneous movements of arm or leg; absent deep tendon reflexes; ankle clonus present; decreased abdominal reflexes. The following investigations were all within normal limits: CBC, urinalysis, X-ray bone survey, CSF, PT and PTT, EEG one week later); brain scan (2 weeks later.)

The patient started speaking by the third day and was relating well with the staff and other children of his age by 1 week, at which time he was able to sit and use his right arm. The right leg remained weak, and he could walk with support only. On discharge he was placed with a foster mother and will be followed closely.

Note in this case the delay in seeking medical attention and a history which fails to account for the findings. The family composition and situation must be associated with a great deal of emotional stress and confusion. Examination of this boy revealed ample evidence of repeated trauma, despite there being no X-ray evidence to suggest old fractures. His behavior and rate of progress in the hospital indicated emotional deprivation in addition to the more obvious physicial abuse.

The second article will outline the development of legislation concerning child abuse, review the efforts of the Advisory Committee on Child Abuse and show how physicians and other health professionals have an important role to play advising legislators on matters relating to the health of the community.

References

1. Kempe, et al: "The Battered Child Syndrome" *JAMA* 181:105-12, No. 1.

2. Gil, David G., Ph.D.: "Physical Abuse of Children: Findings and Implications of a Nationwide Survey" *Pediatrics,* 44:857-64, No. 5 November, 1969 Supplement.

3. Holter, J. ACSW and Friedman, S., M.D.:"Child Abuse: Early Case Finding in an Emergency Department" *Pediatrics,* 42:128-38 No. 1.

4. Stone, N.H.: "Child Abuse by Burning" *Surgical Clinics of North America,* 50:1419-24, December, 1970.

5. Sussman, S. J.: "Skin Manifestations of the Battered Child Syndrome" *Journal of Pediatrics,* 72, No. 1, January, 1968.

Preliminary Experiences with the Treatment of Opiate Addiction by Methadone Withdrawal

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James Ryan, B.A. and Edward J. Rolde, M.D.

In late 1969, the Massachusetts Mental Health Center (MMHC), in cooperation with local, "self-help", drug treatment agencies began a withdrawal program for inpatients from our catchment area addicted to opiates. In 1969 and again in 1970 we carried out a review of the clinical literature describing program experiences with methadone withdrawal. Although there is a growing literature about methadone maintenance, papers describing actual experiences (e.g., techniques, outcome, etc.) with methadone withdrawal are extremely rare. This paper will briefly review the use of methadone for withdrawal from opiate addiction and describe the results to date of our inpatient program.

Methadone

Methadone hydrochloride, which came into use shortly after World War II (Chen[2]), is a relatively long acting (36-48 hrs.) synthetic narcotic with analgesic effects similar to morphine. Isbell and Vogel[6] demonstrated that subcutaneous or intravenous injection of methadone produced euphoria similar to that of morphine, noting that some addicts described the euphoria as more pleasant than that produced by morphine. Moreover, addicts developed tolerance to methadone's analgesic, nauseant, anoretic, sedative, and respiratory depressant

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From the Massachusetts Mental Health Center and Harvard Medical School. Supported in part by USPHS Grant MH 12279.

effects. When the drug was abruptly withdrawn, there was very little evidence for a full blown abstinence syndrome; however, some anxiety, anorexia, insomnia and irritability were observed. Since the abstinence syndrome developed more slowly, was less intense and more prolonged than that seen with other opiate alkaloids, methadone was substituted for morphine in addicted individuals to facilitate withdrawal. Frazer and Isbell[5] showed that oral administration of methadone was as effective as subcutaneous administration in suppressing signs of the abstinence syndrome. Thus it was demonstrated that when methadone was substituted for morphine addiction and then withdrawn slowly over 7 to 10 days, the abstinence syndrome could be greatly alleviated.

The outstanding properties of methadone are its addictive quality, relatively long duration of action, oral administration, and the marked reduction of the abstinence syndrome during withdrawal from this drug.

Methadone addiction, although not as frequent as addiction to morphine or heroin, was seen as a primary diagnosis in about 2 percent of the addicts discharged from the U.S. Public Health Service Hospital in Lexington in 1962. A methadone abuse pattern was thus seen prior to its present use in methadone maintenance programs. In their review of these methadone addicts, Sapira, Ball and Cottrell[10] showed that there was no evidence to support the theory that non-medical use decreases drug seeking or antisocial behavior. Methadone addicts of the mid-1960's had substantial arrest records and multiple hospitalizations, and oral, intravenous, and intramuscular routes of administration were seen. Methadone addicts were noted to have a substantially higher number of second and third drug diagnoses than the drug population at large.

For the non-addict, administration of methadone can produce effects similar to morphine and heroin, and an overdose must be responded to as a medical emergency.

Methadone Maintenance

In a recent series of articles, Nyswander, Dole and associates[3,4,7,8] describe the use of methadone on a prolonged or maintenance basis. They hypothesize that opiate abuse produces a narcotic hunger which can essentially last a lifetime. They have indicated that the oral administration of methadone in doses sufficient to produce dependence can decrease the craving or hunger for heroin, as well as the euphoric high, should heroin be taken concomitantly. They postulate that this effect obtains from the saturation of receptors or blackade of receptor sites specific for opiate alkaloids. In brief, the procedure is to administer methadone *on a daily basis* in increasing dosages until such tolerance is reached (usually about 80 to 120 mg per day), and physical dependence is produced without mental experiences. On this constant dose, the addict presumably escapes the opiate hunger.

In their large series of addicted individuals studied over 5 years, methadone was found to be medically safe in that no deaths occurred as a result of methadone toxicity. When methadone is given on a regular basis, they believe that it is virtually impossible to overdose. Menstrual cycles and pregnancy appear unaffected in methadone maintenance. For the former narcotic user, methadone maintenance has shown no adverse effects on the kidney, liver, respiratory, central nervous system, or bone marrow. In earlier administration, there may be some decreased sexual potency in males, but this has returned over time. Similarly, in the early phases, some oversedation and confusion may appear.

To achieve the desired result in methadone substitution for another opiate addiction, Nyswander says that methadone must be given on a regular basis, in sufficient dosage to produce dependence without euphoria, and over a sufficient period of time—duration as yet to be determined. By decreasing his dosage the addict can succeed in reobtaining the euphoric effects of this or another addictive drug—shifting to an abuse pattern. Thus, to be effective, methadone use must be monitored closely.

Comparison of Methadone Withdrawal and Maintenance

Nyswander[8] in an uncontrolled study claims an 82 percent success rate for the New York Beth Israel Hospital methadone maintenance program, samples selected by the following criteria: age 18 or over, a 2-year addiction history, one drug addiction, and no severe psychiatric problems. Studies of other populations using other approaches by and large do not approach this success rate.

To our knowledge the only relatively controlled comparative study of a methadone withdrawal program versus a prolonged withdrawal program, was carried out in Canada by Paubus and Halliday.[9] Prolonged withdrawal consisted in giving patients oral methadone in doses up to 40 mg for as long as necessary, while regular withdrawal or rewithdrawal was accomplished in a 12-day period. Follow up results after one to five years indicated that forty-one percent of the patients on the withdrawal program and forty-seven percent of the patients on the prolonged program showed signs of positive change. The authors conclude that the overall rates in rehabilitation are not affected by the type of methadone program utilized. They did note however, that older age, hard core addicts seemed to do better on methadone maintenance.

The present programs of Nyswander and colleagues are not comparable in that their samples are more highly selected on the one hand and, on the other, the dose level of methadone maintenance is higher, and follow up is more rigorous.

Patient Sample and Withdrawal Program at the Massachusetts Mental Health Center

In late 1969, the Massachusetts Mental Health Center became increasingly concerned about the problem of drug addiction in our catchment area. We had no specific drug program but believed we should begin work with addicts. Simultaneously, a number of self-help drug treatment programs were being initiated by ex-addicts and non-professionals. Although each program had its own unique combination of therapeutic techniques and group encounters, they all shared the goal of a drug-free state and abstinence for the former addict. They did not utilize, nor wish to use, drug substitution programs such as methadone maintenance. These groups preferred to withdraw the majority of addicts "cold turkey" on the theory that the painful and difficult withdrawal experience would discourage future drug use. They all had very limited 24-hour facilities to use for withdrawal purposes, although some were in the process of developing residence programs. The programs anticipated that some addicts would have a particularly difficult withdrawal. Some would not be able to withdraw without the assistance of a more structured or controlled environment, and others would have superimposed emotional or physical problems making withdrawal difficult. They, therefore, wished to refer to the MMHC those addicts expected to have a difficult withdrawal, while treating the majority in their own program.

The Massachusetts Mental Health Center began evaluating drug addicted individuals for admission to the inpatient services for withdrawal in late 1969. Drug addicted patients received an initial workup, for both psychological and somatic problems, in the Walk-In Service and appropriate cases were admitted to the inpatient services for withdrawal. Admission was considered indicated in the following situations: (1) the patient wanted to be withdrawn from drugs and was referred by a drug dependence program with which the MMHC had a specific working arrangement; (2) the patient was overtly psychotic; (3) the patient was a serious danger to himself or to others; (4) the patient represented a serious behavioral or management problem to himself and/or to those responsible for him.

From 1 August 1969 to 1 August 1970, 28 drug addicted persons were admitted to the MMHC. Of these, 20 were active heroin addicts; five were former heroin addicts, now addicted to methadone; two were also barbiturate addicts; and one was a former heroin addict, considered in danger of relapse. Eighteen were referred from two self-help programs, one from a third self-help drug program, five from private physicians and psychiatrists, two from courts, one from a student health service of a large university, and one from another Boston hospital.

Twenty-four patients were male, ten were black, five married, and two separated or divorced. Fifteen were Catholic and four were Jewish. Seventeen were products of a broken home, five had at least one known alcoholic parent, *and seven were from homes in which at least one other person was a heroin user*. The mean age of the group was 23 years and the mean educational level 11 years. All but three had completed grammar school, twelve completed high school, seven matriculated into and one graduated from college. The mean educational level of blacks in the study was nearly a year lower than that of whites. Twenty-one were unemployed at the time of admission to the hospital.

As obtained in the psychiatric interview, four began heroin and 11 began to use other drugs at age 16 or younger. Only seven began using drugs at age 20 or older, and eight began heroin after this age. Only five patients had been using heroin less than a year at the time of seeking hospitalization; eight had been addicted three years or more. *All but ten had previously attempted withdrawal, but had either been unsuccessful or relapsed later.* Thirteen of the patients had court records for drug related offenses. Heroin intake levels for the 20 on heroin ranged from 3 to 30 bags per day, with the mean of 11.5 bags.

With a sample size of 28, the number of patients is too small to draw statistically significant conclusions, and adequate comparison or control groups were not available. As all patients were screened by a number of filtering processes before admission to the hospital, it is difficult to say that they are representative of any larger groups. However, some general directions can be observed in the population of drug dependent persons who reach the MMHC for treatment. We also offer in conjunction with some of our findings possible hypotheses which should be tested in a larger sample.

The mean age of males was 2.5 years older than females in our sample, and the mean age of blacks was 2.6 years older than that of whites. Since these four subgroups began using heroin at about the same age, this could suggest that whites and females come to treatment somewhat sooner. A number of factors may be involved in this pattern, including relative availability of treatment and social forces predisposing individuals to seek treatment. Thirteen of the patients had used other drugs for at least a year before beginning heroin. Whereas black heroin addicts began heroin six to seven months after first using other drugs, white heroin addicts did not begin heroin until 24 months after their first other drug experience. This may be an indication of greater availability of heroin in the black community, or may reflect that "soft" drug use is not as likely to lead to heroin addiction in the social setting of the white community.

Several factors are substantially correlated with the age at which patients began using heroin. For the group as a whole, the mean age for onset of heroin use was 19.6 years. Patients who had one parent an alcoholic began using heroin 4.8 years earlier than the rest of the study group.* Patients who had another drug user in the family began heroin 3.5 years sooner than the rest of the group.* This finding may imply that the presence of the other drug user influenced the patient to begin heroin sooner, or that if the conditions in the family and neighborhood were sufficiently strong to induce other members of the family to drugs, then they were also sufficient for the index patient to start heroin earlier. Persons from broken homes began heroin 2.3 years earlier than those from stable homes.* Catholics began using heroin 4 years earlier than non-Catholics in the study. Jews on the other hand, began heroin 3.4 years later than the rest of the group. These patterns seen in Catholics and Jews may be attributable to a broad range of social factors rather than to religion alone. A similar trend is seen in the addicts' educational level in that Jews had 2.5 more years of schooling than non-Jews, and the Catholics had 1.7 years less schooling than non-Catholics. This parallel does not, however, continue when racial comparisons are made.

Results

The 28 patients were admitted to one of three inpatient wards at the MMHC, an open door hospital. Addicts were mixed in with psychiatric patients on the unlocked wards, as no separate facility was available for treatment. Responsibility for the patient's inhospital treatment program rested with his doctor, a supervised first-year resident psychiatrist, and with the staff of the ward to which he was assigned. It was expected that for those patients referred from a drug dependence program, the referring agency would be available to help with the patient's treatment while in the hospital and after discharge, when the patient would return to the local program.

While in the hospital, methadone was prescribed to heroin addicts during the withdrawal period. Three slightly different prescribing patterns were observed on the three inpatient services: (1) Administration of sufficient methadone to alleviate symptoms once the patient begins withdrawal symptoms, increasing dosage on a regular basis until the patient is asymptomatic. Methadone is withheld until the first signs of withdrawal are seen such as sweating, rhinorrhea, dilated pupils and restlessness. Then 10-20 mgs of methadone are given orally and repeated when symptoms recur. A regimen is then calculated based on a 24 to 48 hour total dose. (2) Initiation of methadone immediately at a dosage level proportionate to the patient's heroin habit as indicated by the patient or referral agency. Dosage is estimated usually on 10 mgs of methadone per "bag" of heroin or approximately 1 mg of methadone to 1 or 2 mgs of heroin. (3) Initiation of treatment with methadone at a low level, 10 to 20 mgs, increasing dosage until narcotic effects are noticed, then backing off, having calculated a 24 hour daily dose. No definite conclusions could be drawn as to which of the above methods was most effective in assuring patient comfort while guarding against excessive levels of medication. In discussion with resident psychiatrists and staff, it appeared that initiation of methadone at a dosage level proportionate to the patient's habit (i.e., method number 2) was the most efficient in terms of practical management, and there did not appear to be any contraindications to this method. However, it should be noted that a somewhat higher initial dose of methadone was arrived at by this method. Once a level of methadone was arrived at, it was then reduced at the rate of 5-10 mgs per days until the patient was completely withdrawn from drugs.

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* Statistical analyses were based on the Mann Whitney U Test of statistical significance. As already noted, the sample size is small, making statistical tests of significance of limited value, but they are included here to further indicate the direction of these findings. All starred differences were statistically significant ($p < .025$).

Twenty-three patients received methadone in the course of their treatment. Initial methadone levels ranged up to 150 mgs per day, with the majority receiving between 40 and 60 mgs. Twenty patients completed methadone withdrawal while in the hospital. Patients completing a methadone withdrawal schedule received the drug for an average of 8.5 days (mean and median).

The average length of hospitalization for patients was about two weeks (median 12.5, mean 17.9 days). Eighteen patients completed treatment and were discharged to the referring agency or agent. When referred by the self-help group, arrangements were usually made for the patient to be met by someone from the referral agency, so that he would not be alone during the initial period after discharge. Three patients signed out against medical advice, four escaped, two were discharged for failing to make use of the hospital, and one was treated as an outpatient as he had hepatitis.

At the close of our pilot study, 1 August 1970, essentially one year from the onset, ten patients were known to be drug free, ten were known to have resumed using drugs, seven were lost to follow-up and one was committed to prison. Of the 20 patients completing methadone withdrawal at the hospital, nine were known to be drug free, seven were using drugs again, three were lost to follow-up, and one was in jail. Similarly, of the 18 patients who completed hospital treatment, nine were drug free, seven were using drugs again, one was lost to follow-up and one was in jail. Thus, for the sample as a whole, 36 percent were drug free; for those completing the hospital methadone withdrawal program, 45 percent were drug free; and for those completing the hospital treatment program, 50 percent were drug free. There appears to be a tendency for drug free state to be correlated with both completion of methadone withdrawal and completion of hospital treatment.

A comparison of the two major self-help programs who referred 18 of the 28 patients revealed no substantial differences in terms of follow-up drug status. For one of the programs, 30 percent of their referrals were drug free, and for the other, 50 percent. However, the latter program had substantially more of the recent referrals which could have increased the relative number of drug free individuals at the time of follow-up. A larger sample over time would be needed to establish the relative or comparative advantages, if any, of various self-help programs using this methadone withdrawal program.

Finally the major factor which correlated the recidivism was the time since discharge from the hospital. For those participants who were still drug free at the close of the present study, the mean time since discharge was 75 days. For those who returned to drugs the mean time was 114 days. This indicates that the most recently discharged patients were most likely to be drug free and shows a compelling need for a continued follow-up.

Discussion

Our results to date certainly do not indicate a success rate nearly approaching that of Nyswander, Dole and colleagues. It is evident that their admission criteria would make a substantial number of our patients ineligible for their program (i.e., those patients in our sample who were under 18, or who presented with a mixed addiction, or who had significant emotional illness would have been excluded from their population.) The patients in our program clearly represent a more difficult or refractory group to begin with, since the majority of our referrals were patients that the self-help programs could not handle.

The evaluation of any drug treatment program, such as this limited one at the MMHC, is a complex problem. While the success of an overall program can, to some extent, be gauged in terms of the ratio of drug free to drug dependent individuals at a defined interval, the success for a specific addict must take a number of factors into account: (1) Has the individual worked sufficiently to support himself and/or his family? (2) Has he developed social acquaintances outside of the world of drugs? (3) Has he established or re-established family ties? (4) Has he broken his patterns of criminal behavior? (5) Has he a sense of self-worth or the feeling that some meaning to his life has been restored? These and other questions must be asked when evaluating an addict's rehabilitation. Such criteria are based on a view that the addict can become a productive member of society. The Council on Mental Health[1] of the American Medical Association includes among their criteria for recovery from drug dependence ". . . he does not suffer from a significant general social and economic disability or incapacity." Some clinicians and perhaps some addicts would argue that these goals are unrealistic. Some addicts have severe character disorders manifested as passivity, dependency, and orality. A more reasonable goal for such addicts might be to accept the passive-dependency of this subgroup and hope to minimize their counterproductivity.

What would seem indicated at this time would be a continued openness to experiment with and study a variety of treatment programs—methadone withdrawal, methadone maintenance, cyclazozine, residential facilities, confrontation and ex-addict programs and vocationally-oriented programs. Individual psychotherapy, even though it may have limited public health value, should also be reevaluated. Much of the negative thinking about the value of individual psychotherapy has come from its failure to help so-called "hard core" addicts, often black and often from ghetto backgrounds. Individual psychotherapy in conjunction with methadone maintenance has not been studied adequately, and the role of individual psychotherapy alone has not been systematically evaluated in young and/or non-ghetto cohorts. Such comparative studies, controlled when possible, will tell us in an increasingly specific manner which types of addicted individuals can benefit from which programs or combinations of programs.

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Primary Reticulum Cell Sarcoma Of The Brain Stem

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Abstract

A case of primary reticulum cell sarcoma of the brain stem is presented. This is a rare neoplasm and since Yuile[1] reported the first case in 1938 fewer than 100 cases have been cited. There is no agreement as to which cells of the reticuloendothelial system in the brain give rise to the neoplasm and consequently it has been described by many different terms including: primary reticulum cell sarcoma, microglioma, microgliomatosis of the brain, perivascular sarcoma, perithelioma and primary mesenchymal tumor. There is general agreement, however, regarding the microscopic morphology of the tumor and this case presents a typical example. Also noteworthy is the manner in which the tumor presented clinically. It originated in the mesencephalon causing an oculomotor nerve paralysis and crossed hemiparesis (Weber's syndrome). This syndrome is usually associated with infarction of the ventral mesencephalon secondary to thrombosis of a perforating branch of the basilar artery.

Case Report

The patient, a 48 year old white man, was admitted to the Norwalk Hospital with a one week history of left hemiparesis and right third nerve paralysis. Over the previous two

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months he had noted increasing unsteadiness of gait and memory loss making it impossible for him to continue work as a business executive.

The only abnormalities on physical examination were confined to the nervous system. The patient was confused and unable to subtract serial sevens. Ptosis of the right eyelid was present and the right pupil was dilated and did not react to light or accommodation. There was a moderate left hemiparesis that did not involve the face. Deep tendon reflexes were hyperactive on the left in both the upper and lower extremities. Babinski's sign was present on the left. No other neurologic abnormalities were present.

Routine laboratory tests were all within normal limits including hemogram, urinalysis, and serum electrolytes. Roentgenograms of the skull and chest revealed no abnormalities. An EEG was within normal limits. Lumbar puncture revealed normal pressure, a protein of 243 mgm % and 3 lymphocytes. A ventriculogram showed slight dilatation of the lateral and third ventricles. The cerebral aqueduct and fourth ventricle were not visualized. Ventricular cerebrospinal fluid protein was 56 mgm %. Bilateral carotid arteriograms were unremarkable except for minimal stretching of the pericollosal arteries secondary to slight dilatation of the lateral ventricles.

The patient was given dexamethasone 10 mgm t.i.d. and gradually improved over the next 6 days with clearing of his sensorium and lessening of the left hemiparesis. The improvement was temporary, however, and during the ensuing 6 weeks the left hemiparesis grew worse and the level of consciousness gradually deteriorated to coma. He died with acute bronchopneumonia.

With the exception of extensive necrotizing bilateral pneumonia, all of the significant abnormalities found at autopsy were limited to the brain. Grossly the brain appeared normal on all surfaces. After sectioning, however, an extensive tumor of the brain stem was evident, extending from the floor of the posterior portion of the third ventricle down through the subthalamus, mesencephalon, and pons (Figure 1 and Figure 2).

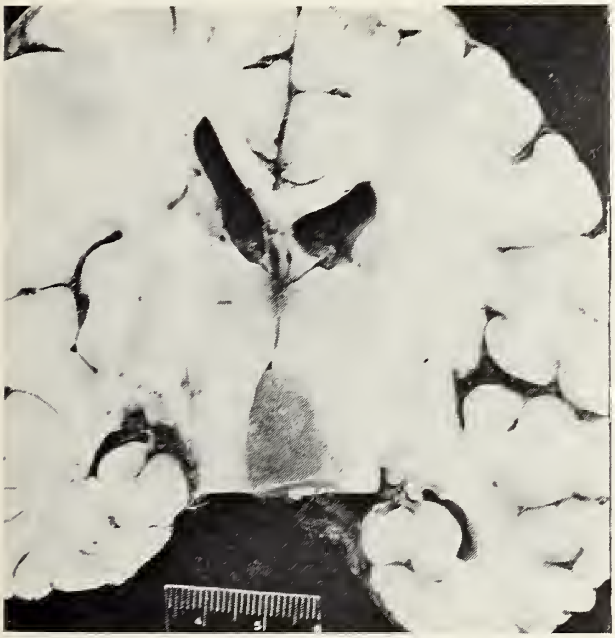

Figure 1

Coronal section through thalamus showing tumor extending from the mesencephalon into subthalamus and floor of third ventricle.

Microscopically the tumor was a typical reticulum cell sarcoma. It was composed of medium to small round cells lying in clusters with no specific configuration. The cytoplasm was pale and stained poorly with hematoxylin and eosin. The nuclei tended to be vesicular and fairly regular in shape with nucleoli and considerable chromatin clumping (Figure 3). Associated with the neoplastic cells were diffusely infiltrating lymphocytes and plasma cells. Stain for reticulin was strongly positive throughout the tumor (Figure 4). Mucin stain demonstrated no intracellular mucin and PTAH stain was negative for glial fibrils.

Discussion

Primary neoplasms of the brain arising from the reticuloendothelial system have been described by many terms including: reticulum cell sarcoma,[2] microglioma,[3] microgliomatosis,[4] perithelioma,[5] reticuloendothelial sarcoma,[6] and primary mesenchymal tumor of the brain.[7] Various terms are used not because there is disagreement as to the general histologic appearance of the tumor but rather because there is no consensus as to which of the three types of cells representing the reticuloendothelial system in the brain gives rise to the neoplasm. Cells belonging to the reticuloendothelial system that are normally found in brain include microglia, perivascular histocytes (contained in the adventitial sheaths of the cerebral blood vessels), and fixed macrophages (contained in the connective tissue that forms the boundaries of the Vischow-Robin spaces).

Adams and Jackson[8] were able to impregnate

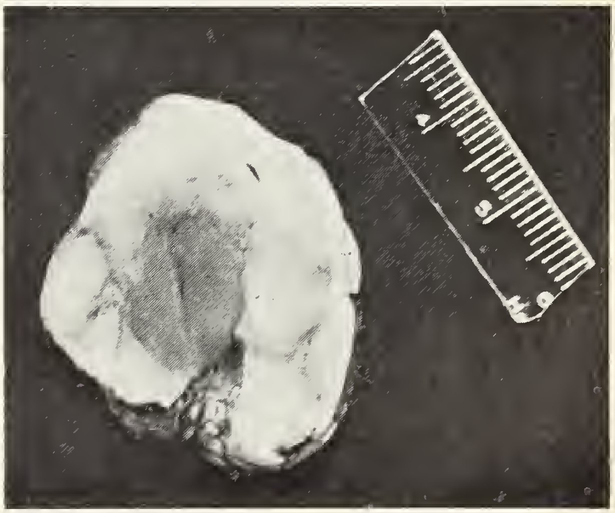

Figure 2

Transverse section through mesencephalon showing tumor extending into the right cerebral peduncle.

four intracerebral reticulum cell sarcomas with a silver carbonate stain developed primarily for the recognition of microglia and on the basis of such tenuous evidence suggested that the tumors were microglial in origin. Peison and Voris[9] on the other hand, in reporting a morphologically similar primary neoplasm of the brain concluded that the tumor arose from adventitial histiocytes because it would not impregnate with Hortega's silver carbonate method for microglia. Because Hortega's method is by no means specific when staining neoplastic cells such a conclusion is open to serious question. Dunning and Furth[10] have concluded that histiocytes and microglia are identical functionally and morphologically and constitute a single cell type. If indeed this is true, the controversy over which cell gives rise to primary reticulum cell sarcoma of the brain is meaningless. Because it is probable that any of the three types of cells can give rise to primary reticulum cell sarcoma within the brain terms implying a specific cell of origin such as microglioma or perithelioma should be abandoned.

The manner in which the tumor manifested its presence clinically is noteworthy. At the time of admission the patient had a left hemiparesis and right third nerve palsy, Weber's syndrome. This is usually caused by thrombosis of one or more of the short perforating branches of the basilar artery to the paramedian area of the mesencephalon resulting in destruction of corticospinal fibers in the cerebral peduncle and oculomotor nerve fibers as they pass from the oculomotor nucleus ventrally to exit in the interpeducular fossa. The neoplasm precisely mimicked the vascular syndrome by occupying the area in the mesencephalon usually infarcted (Figure 2). The slow steady progression of the patient's neurologic deficit and the temporary but remarkable improvement after the administration of dexamethasone were, however, more characteristic of neoplasm than stroke.

Acknowledgment

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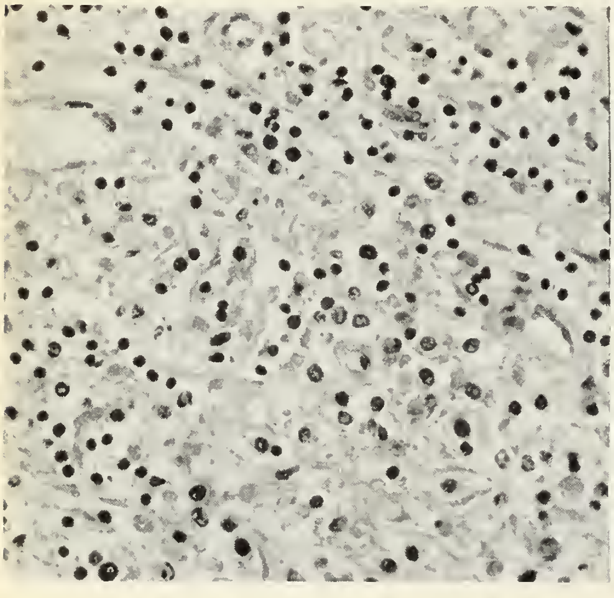

Figure 3

Tumor consisting of cells with small round darkly staining nuclei and pale cytoplasm. H+E X400.

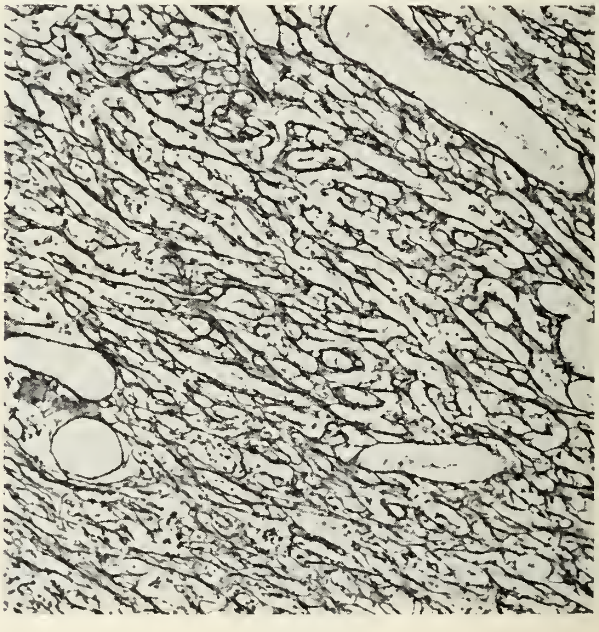

Figure 4

Tumor showing extensive production of reticulin throughout. Reticulin stain X 100.

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Human Rabies Prevention in Connecticut

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Introduction

The large reservior of rabies among wild animals throughout the United States provides a variable but constant threat to humans and domestic animals and necessitates continued surveillance and knowledge of appropriate preventive measures. In the United States approximately 500,000 people are bitten by animals each year and about 30,000 of these receive rabies prophylaxis.[1] A large portion of such treatments are unnecessary when considered in the light of the nature of the exposure and the regional epidemiology of the disease. Even more unfortunate, many actually requiring treatment receive therapy which is inadequate in timing, dose or type.

Despite these shortcomings, the incidence of human rabies in the United States is remarkably low. There was one fatality in 1969 and 3 cases in 1970, one of whom may represent the first reported recovery from Central Nervous System (CNS) rabies.[2]

Our purpose is to review briefly the epidemiology of rabies, its epidemiology in Connecticut, what is known about the pathogenesis of the disease, and to offer recommendations for an approach to proper evaluation and management of individuals with possible exposure in Connecticut.

Epidemiology

Carnivorous and omnivorous animals are the prime vectors of the disease. Prior to World War II, dogs were the major source of human rabies in the United States, but effective dog control laws and the development of effective animal vaccines and vaccination programs have dramatically reduced the incidence of pet rabies. As a result wild animals are now the main source of human disease.[1]

Excretion of virus and the capacity to infect others does not occur until the virus is localized in the salivary glands.[3] This localization takes place late in the course of illness at a time when the CNS disease is sufficiently advanced that death prevents the animal from becoming a chronic vector of the disease. Bats appear to be an exception to this usual natural history. Bats are known to excrete rabies virus for extended periods without overt illness.[4] During the past three and one-half years, the only proven rabid animals in Connecticut and Massachusetts have been bats.[5-7] It is suspected that they may be a major animal reservoir of rabies virus, providing a source for sporadic sylvatic and human disease. It is also becoming apparent that bats carry other neurotropic rabies-like viruses which may produce human disease. These viruses show complete crossover with rabies when fluorescent antibody serological techniques commonly used in diagnostic laboratories are analyzed. Moreover, these are heterologous viruses which may explain some past treatment failures, since protection may not be provided by rabies vaccine and sera.[8] Small rodents may contract the disease but appear

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more resistant to infection and are not usually vectors except in areas of high endemicity.[4,9]

In other neighboring New England states and in New York, the fox is the most commonly reported rabid animal.[5-7] However, reports over the last three and one-half years have included, in descending order of frequency, skunks, cattle, dogs, racoons and cats.

Pathogenesis

The course of rabies infection is well-known once CNS disease becomes apparent. The incubation period is, however, highly variable and the route to the CNS is not clearly defined. It is assumed that the virus invades and ascends peripheral nerves to the CNS, but viremia following introduction of a suitable inoculum may occur. Rabies has been contracted by humans and test animals in bat caves, presumably from inhalation of virus laden bat guano dust.[10] Animal studies have demonstrated that the disease can occur following ingestion of virus.[11] Moreover, rabies virus has been demonstrated in circulating lymphocytes after inoculation intracerebrally, intraperitoneally, and intramuscularly.[12] Virus has been detected in the CNS 24 to 48 hours following intramuscular injection.[13] Whatever the natural route to the CNS, it takes ten days to a year or more for CNS symptoms to appear in the human. The incubation period has been roughly related to the proximity of the wound to the brain.

There is some evidence that irreversible invasion of the host takes at least 24 hours, presumably the time required for the virus to invade peripheral nerves or to circulate and invade the CNS. Once the virus is "fixed" to nervous tissue, no measures are effective in preventing the ultimate progression of the disease.[3,14]

Therapeutic Problems

The efficacy of vaccine therapy has been exceptionally difficult to determine. The intense anxiety surrounding a patient bitten by a suspected rabid animal has resulted in the use, when available, of rabies vaccine in every patient. In 1953, 32 people were bitten by an infectious rabid wolf in Iran. Only 6 received treatment, but of the type considered inadequate by present standards. Fifteen died giving a fatality rate of 47%. In 1954 analysis of another group of cases in Iran that had received satisfactory therapy with wound care and Semple vaccine, revealed that adequately treated patients with wounds of the head and neck had a mortality rate as high as 40%, whereas the mortality rate among patients with wounds on the trunk or extremities or with minor wounds of the head and neck was 10%. The fatality rate for all patients in this study with proven rabies exposure and adequate treatment was 25%.[15] These reports confirm other observations that the extent and location of the wound are major determinants of the subsequent development of disease. Moreover, shortly after Pasteur's initial successes, antiserum from hyperimmunized animals was shown to exert a protective effect. More recent studies in experimental animals and in exposed humans have indicated greater effectiveness of hyperimmune antiserum and vaccination for post-exposure treatment.[3,14-16] These facts suggest that active immunization alone is not optimal for post-exposure treatment.

Complications of Treatment

Vaccine: A major impetus to develop new approaches to antirabies therapy has been the occurrence of vaccine induced allergic encephalomyelitis when crude nervous system preparations have been used. The present killed virus vaccine prepared in duck embryos (DEV) has reduced this complication dramatically, but has not entirely eliminated the risk; it has noticeably reduced the antibody response as compared to the older Semple, Rabbit Brain vaccine.[17] Current work on vaccines prepared in tissue cultures indicates that safer and more effective preparations may be soon available. The duck embryo vaccine remains one of the crudest of biological preparations currently used. Most patients will develop local reactions consisting of edema, erythema and tenderness at the site of inoculation. Serious systemic allergic reactions are rare.

Antiserum: Antiserum prepared in horses is commercially available. Unfortunately, its use is accompanied by the frequent occurrence of serum sickness and the threat of immediate severe anaphylactic reactions. The incidence of serum sickness is 16% overall and is 46% among those patients over 15 years of age.[18] Although this morbidity is high, the complication can usually be effectively treated with antihistamines and aspirin.

Immediate anaphylaxis is always a risk and testing for potential reactors with intra-dermal tests as outlined by the manufacturer is mandatory.

Despite these problems, the effectiveness of antiserum in rabies is of such importance that immediate use in the known exposed patient should not be delayed or withheld. A human hyper-immune serum under development and testing should provide an effective prophylaxis associated with fewer complications.[19]

Approach to the Individual Case

Table 1, adapted from the 1970 report of the Committee on Infectious Diseases of the American Academy of Pediatrics, outlines a reasonable approach to the problem.

TABLE 1

PROTOCOL FOR POST-EXPOSURE RABIES PROPHYLAXIS

Biting animal *Species*	*Status at Time of Attack*	*No lesion*	*Mild*[1]	*Severe*[1]
Dog or cat	Healthy	None	None	None[2]
	Signs Suggestive of Rabies	None	S&V[2]	S&V[2]
	Escaped or Unknown	None	S&V	S&V
	Rabid	None	S&V	S&V
Skunk, Fox Racoon, Bat	Regard as Rabid	None	S&V	S&V

S = Antirabies Serum
V = Rabies Vaccine (Duck Embryo)

[1] Definitions: Mild exposure—scratches, lacerations, abrasions or single bites on areas of the body other than head, face, neck, upper extremities.

Severe exposure—multiple or deep puncture wounds; any bites or broken skin on head, face, neck, or upper extremities; contamination of broken skin with rabid saliva.

[2] With unprovoked severe bites by apparently healthy animals or animals appearing sick, we recommend that the animals be sacrificed and the brain examined pathologically; if evidence for rabies is present on examination, treatment with S&V should begin immediately.

Any bite by a wild animal known to be a probable local rabies vector (in Connecticut the bat and probably the fox and the skunk) demands immediate institution of treatment with both antiserum and vaccine. Similarly, unprovoked bites by stray animals known to be possible vectors (e.g. racoons) in the region, that have escaped and cannot be observed, constitute a potential serious exposure and the patient should be considered for immediate treatment. Treatment delayed beyond 24 hours is known to be less effective.[3] Provoked bites by squirrels and other rodents in Connecticut probably are not indications for treatment at the present time.

Because of the ubiquity of bites by "friendly" pet animals, additional information about the incident and the animal is essential before starting rabies prophylaxis in view of the low rabies endemicity in this state. A rabies vaccination within 2 years is regarded as providing satisfactory protection for dogs, but immunity varies with the type of vaccine used, and a consultation with the veterinarian is indicated.* Vaccination of pets should be left to qualified individuals since some vaccines available may cause infectious rabies if incorrectly used in the wrong species (including man, the inadvertent recipient as a result of a wiggling pet).[1]

Unprovoked bites by apparently healthy dogs are suspicious and require quarantine and observation of the animals for 10 days, even if the animal has a valid vaccination certificate. Prophylactic treatment for the patient may be withheld as long as local wound care is adequate and the animal remains healthy. If the wounds are severe, on the head or neck, or if the animal is sick, the animal should be forwarded to the health authorities immediately for sacrifice and pathologic examination. An answer may be available from the state laboratory within 24 hours. If further delay is unavoidable, consideration should be given to immediate initiation of both serum and vaccine therapy which should be continued until the results of examination are available.

Minor lacerations of the extremities require local wound care, diligent search into the background of the accident and expectant management of the patient and the animal. Indirect contact, including licking of the unbroken skin and soilage of the clothes with saliva does not constitute an exposure, even when a known rabid animal is involved. An exception may be considered in a spelunker's exposure to bat secretions, but pre-exposure prophylaxis for such individuals is recommended and outlined below.

Treatment Protocol

The type of treatment recommended, if required, is logically both antiserum and vaccine. The efficacy of antiserum is clear and it should not be withheld. The use of the presently available DEV alone is not justified in our minds at the present.

Local care: Meticulous care of the wound is remarkably effective in eliminating or reducing the viral inoculum. Debridement and deep wound irrigation for at least 15 minutes is indicated. Quaternary ammonium compounds (zephiran) and 20% soap solutions are virucidal and should be used liberally, but not together since soap inactivates the quaternary ammonium compounds. The use of topical lidocaine (xylocaine) will help to alleviate pain during these manipulations. Tetnus prophylaxis should be given when indicated.

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* Pet animals known to have been bitten by a rabid animal should be destroyed unless vaccinated against rabies in the past two years. Even if vaccinated the animal should be revaccinated and strictly quarantined for six months; unless the owner protests, it seems more kind, wise and less expensive to destroy the animal.

Antiserum: Antiserum is given in a single dose of 40 units per kilogram of body weight. One half the total dose is injected around and into the wound. The remainder is given intramuscularly. Preliminary testing for hypersensitivity to horse serum is mandatory. Even when the test is negative, epinephrine should be available and at hand for use in immediate reactions.

Vaccine: Duck embryo killed virus vaccine should be injected subcutaneously in the abdominal wall or other accessable sites. Either of two schedules may be used depending on the severity of exposure (Table 2). Since there is evidence that endogenous antibody is not adequate until the 4th week and delayed by the use of antiserum, we favor the second schedule.[16,19]

TABLE 2

SCHEDULES FOR DUCK EMBRYO VACCINE

Schedule 1		
	First 7 days	2 ml/day
	Next 7 days	1 ml/day
	10 days later	1 ml
	20 days later	1 ml
	Total dose	23 ml
Schedule 2		
	First 7 days	2 ml/day
	Next 14 days	1 ml/day
	10 days later	1 ml
	20 days later	1 ml
	Total dose	30 ml

Pre-exposure prophylaxis: Individuals (veterinarians, dog control officers, game wardens, spelunkers, and laboratory workers) whose occupations involve potential exposure to rabid animals or rabies virus should receive immunization. Two doses of 1 ml of DEV should be given at an interval of one month, followed by a 1 ml booster dose 7 months later. To determine the antibody response, serum must be submitted to the State Laboratory for antibody determinations after this series because 5 to 10% of individuals will not be immune. Such individuals should have further boosters at monthly intervals until adequate antibody levels are obtained. Protection, as measured serologically, is variable in persistance but usually lasts for 1 to 2 years. Boosters should be given at 1 to 2 year intervals for as long as the individual is at risk. Rabies exposure in satisfactorily immunized individuals requires 1 ml boosters daily for 2 days followed by a 1 ml dose one week later. No antiserum is required for these individuals. If immunization is not current, the patient should be considered unprotected and treated as an unimmunized individual.

Summary

Animal rabies continues to be a threat to humans. In Connecticut the major reservoir is the bat; however, neighboring states continue to have rabies in foxes, skunks and dogs. The decision to treat a patient bitten by an animal is dependent upon the location and severity of the wounds and the species and health of the animal. Adequate post-exposure treatment is three-fold: meticulous wound care, antirabies serum, and rabies vaccine. Pre-exposure prophylaxis for individuals at high risk is recommended.

Addendum

Since this paper was submitted for publication, further clinical trials with human Rabies Immune Globulin have been published.* Adequate levels of passively transferred serum neutralizing antibody were obtained with 20 international units/kg body weight of human Rabies Immune Globulin. Higher doses interfered with active immunization utilizing duck embryo Rabies Vaccine.

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Paradoxes

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Food is abundant: malnutrition exists.

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Educational opportunities abound; why is there illiteracy?

Technology soars: the ghettos decay.

The population continues to grow: crime rates grow faster.

Demands for change find few echoing plans for change.

—JAMA, September 13, 1971, Vol. 217, No. 11.

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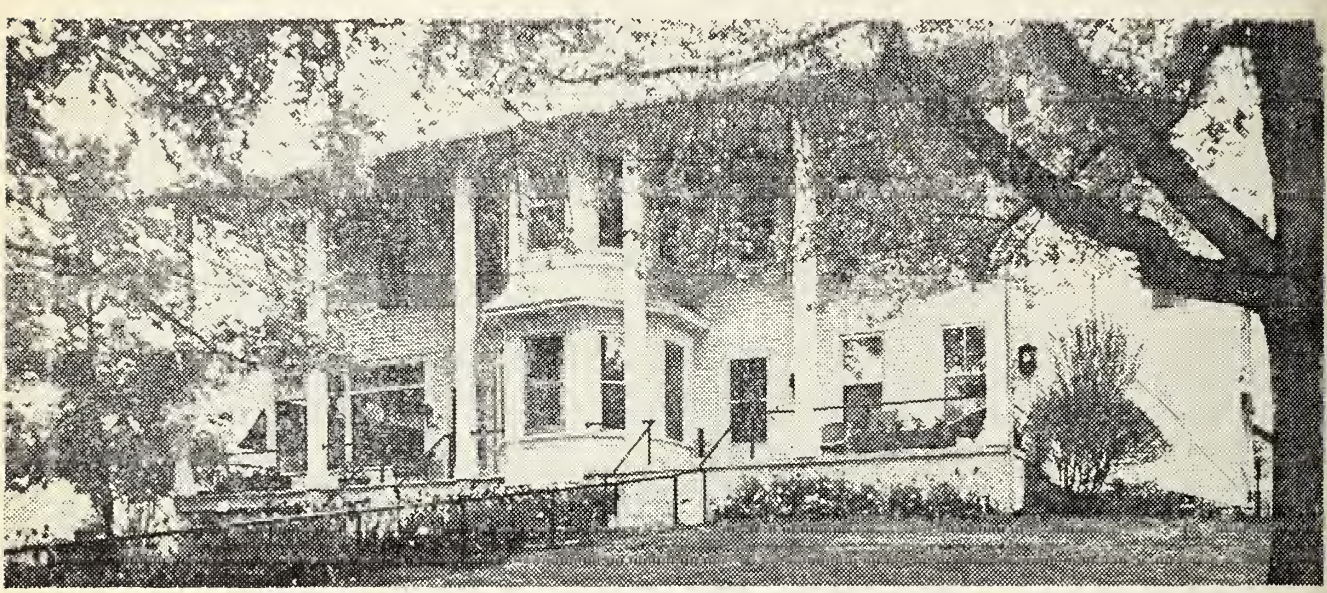

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Connecticut Medicine

Editorials

Science Tools: Image Analysis

This is a method of optical scanning with digital computers to assist or replace human judgment in medical diagnosis. Efforts have been made to develop techniques for recognizing and classifying blood cells by typing chromosomes and identifying cancer cells. These image analysis techniques have now been extended to radiology and in one of the first such applications, doctors and engineers at the University of Missouri have demonstrated the feasibility of diagnosing rheumatic heart disease with an automatic system for analyzing chest X-ray images. Trials with the image analysis system showed that its diagnosis was more accurate on the average than that of a panel of radiologists.

The basic technique involves the conversion of an image whether a photomicrograph or a cell or an X-ray film to a two-dimensional array of numbers each of which represents the "grayness" of the image that is the gradations of light and dark on the film at a particular location. The camera can distinguish 64 shades of gray and is capable of resolving an image into an array as large as 1024 by 1024. In the rheumatic heart application only 256 by 256 data points are taken. Once the X-ray image has been converted to a series of grayness values the data is processed with a computer for the purpose of identifying and extracting the features of the image.

Once the heart has been located and its outline determined the computer extracts information on which diagnostic decisions can be made. In a particular case the computer obtains the measurements from an X-ray image, decides on the basis of the probability table whether the heart is normal or abnormal and if abnormal selects one or more of four different types of rheumatic abnormality as the most probable diagnosis.

The image analysis system was tested against a panel of ten radiologists on a series of 135 patients for which the correct diagnosis was known. The radiologists using both front and lateral X-rays made individual diagnoses whereas the computer used only the frontal X-ray. The overall accuracy of correct diagnosis by the radiologists was 62 percent as compared to an accuracy of 73 percent for the computer. The computer's accuracy was also higher than that of any individual radiologist. In determining the normal heart, both the radiologists and the computer achieved a comparable accuracy but the radiologist had a greater tendency to make false positive identifications and the computer was more accurate in placing abnormal cases into the correct class of rheumatic heart disease. The performance of the image analysis system and the accuracy of the fully automated diagnosis thus established the feasibility of using image analysis for this medical application.

In rural medical practice a central facility equipped with a computer could process and evaluate X-rays from areas where trained radiologists are scarce. Image analysis techniques may eventually provide a consistent standard of comparison for what is often widely varying clinical judgment and thus lead to means of monitoring and supplementing medical diagnostic practice. The cost of the system is still somewhat high (the analysis of each X-ray requires about 3 minutes of computer time on an IBM 360/50), but as part of a network serving large numbers of users, the system may become economically feasible.

The Missouri scientists have begun work on other radiological applications of image analysis including an attempt to diagnose congenital heart damage from chest X-rays and efforts to identify and classify bone tumors from X-ray films. They are also trying to develop means of evaluating coal miners' pneumoconiosis.

Elswhere other medical applications are being pursued, including methods to automate differential blood counts to characterize chromosomes for karyotype analysis and for research in cytogenetics and to identify cancer cells. Mendelsohn's group at the University of Pennsylvania—analyzing the DNA content of chromosomes by image analysis techniques.

A group headed by George Wied of the University of Chicago and Peter Bartels of the University of Arizona is trying to automate the examination of endometrial cells for cervical cancer. They hope by this means to improve the reliability of diagnosis of early malignant and pre-malignant tumor cells and by modeling the evaluation of the disease to make objective comparisons of different therapies.

The image analysis techniques used in all these applications are basically similar to those that have now been applied to rheumatic heart disease. Perhaps the most significant feature of these efforts is their interdisciplinary nature. In the case of the Missouri group, it involved the sustained cooperation of electrical engineers and radiologists over a period of six years. Such a cooperation may eventually lead to improvement in the practice of medicine and make its benefits more widely available.—L.H.N.

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Vitamin E.

Originally when vitamins were discovered a wave of enthusiasm about their value in clinical medicine spread to engulf every patient, and every doctor in every disease. The pendulum than swung back to the opposite extreme where it was stated that all people eating "properly" cannot be vitamin deficient. In consequence, we probably missed many opportunities to assist some of our patients to achieve a more healthful nutritional state, particularly of the brain and peripheral nervous system long before anemia becomes the signal for the search for pernicious anemia.

We now find a similar story about vitamin E, which was discovered in 1922. Since its discovery, there has been a frustrating searching for effects of its deficiency and for its therapeutic utility. Originally, it was found to be a dietary substance essential for normal reproduction in rats. This initiated a long period of extensive trials of vitamin E therapy for threatened abortion for menopausal disturbances and disorders of sexual function in man. Failure of these therapies is now a matter of record. Similar lack of success followed other attempts at extrapolating observations from animals to man. Skeletal and cardiac muscle abnormalities observed in animals deficient in vitamin E have led to futile trials in human sufferers from muscular dystrophies and various cardiovascular disorders.[1]

On firmer ground is the association of vitamin E deficiency with anemia. For example, humans on diets deficient in this vitamin will have more ready hemolysis of their red cells when exposed to antioxidants and their red cell survival times are definitely shorter than those of normal persons. In premature infants, Ritchie[2] reported on seven such patients with widespread edema and anemia which was hemolytic and associated with thrombocytosis and who responded to vitamin E 75 mg per day. The vitamin was not effective if also given simultaneously with iron because iron destroyed the vitamin in the gastrointestinal tract. They found that the deficiency was due to the infants receiving a synthetic diet which was low in vitamin E. Breast fed infants by contrast never developed the syndrome. Two lessons were learned from Ritchie's experience: vitamin E may not be taken with iron, and the anemia in the syndrome he described in vitamin E deficient infants may be merely the tip of the iceberg of a much more profound and widespread disturbance.

On firm ground is the association of vitamin E deficiency with a deficiency in heme synthesis even though it is difficult to pinpoint the rate of vitamin E deficiency in the etiology of other forms of anemia, because of deficiencies of other vitamins and nutrients invariably present in anemic patients under investigation. A more precise assessment of vitamin E has been recently presented by Nair, et al[3] on its effect on porphyrin metabolism and the effectiveness of this vitamin in the treatment of Porphyria Cutanea Tarda. They report successful control of symptoms and reduction of the urinary excretion of porphyrins and their precursors in preventing experimental porphyria in the rat as well as successful treatment of patients with the disease.

Their cases had low pretreatment values for vitamin E which rose gradually over a period of weeks on treatment with daily doses of vitamin E of 100 mg. Initially elevated urinary excretion of intermediate heme products which reflected the overproduction of heme precursors decreased to normal levels and symptomatic improvement accompanied these biochemical changes. Since the biochemical abnormalities of porphyria which are corrected by vitamin E involve intermediate metabolites in the formation of heme and heme proteins, the key to the etiology of porphyria and to its response to vitamin E must be in one or more regulatory mechanisms of this biosynthesis.

Whether as Nair and his associates suggest that vitamin E acts by blocking amino-levulinic acid-synthetase or by correcting deranged feedback control of heme formation, or by other less direct mechanisms is still unknown. However, anemia in vitamin E deficient infants and patients with porphyria may be merely the tip of the iceberg of a much more profound and widespread disturbance.[4] There probably will be more to come. We must not be too complacent about deficiencies of vitamins not taking place merely because people are on a presumed "proper" diet. —L.H.N.

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Oral Anticoagulation

After more than 25 years of use and numerous clinical trials of greater or lesser merit, the place of oral anticoagulants in the management of thrombo-embolic disease remains uncertain. After an exhaustive and careful review of the use of anticoagulants in various clinical situations Douglas[1] has concluded that they may be of some benefit in preventing deep vein thrombosis and pulmonary embolism in patients who are particularly at risk as the elderly with fractured long bones of the legs or those in whom prolonged bed rest and immobility are anticipated. In disorders of arteries, however, the evidence favors by only a narrow margin the use of these drugs on a long term basis, provided that the test of prothrombin is reliable and provided also that the usual contraindications to anticoagulant therapy have been properly excluded.

The use of oral anticoagulants in the management of acute myocardial infarctions already under heavy criticism was shown to produce no significant reduction in mortality of a large group of patients in multicenter study sponsored by the Medical Research Council in Great Britain.[2] The numerous investigations of oral anticoagulant therapy have been plagued with problems and differences of opinion concerning the statistical clinical and laboratory aspects. One of the problems in the laboratory control of anticoagulation has been the purity of the various thromboplastins used to estimate the prothrombin time.

There also enters into the problem the variety of drugs which influence the effectiveness of coumarin drugs in producing hypocoagulability. Some are known to enhance coumarin action. Phenylbutazone clofibrate, quinidine, salicylates and dilantin all enhance coumarin action. Others such as the barbiturates and chloral hydral reduce the activity of coumarins. Antibiotics in particular may indirectly enhance the activity of coumarin drugs by inhibiting vitamin K synthesis by intestinal microorganisms. Care must, therefore, be exercised in changing drug regimens while patients are receiving anticoagulants lest their treatment becomes either ineffective or dangerous.

There are also inborn variations in resistance to coumarin drugs. This is well known in rodents and is also a considerable factor in some humans who are found to be highly resistant, a trait that is inherited as an autosomal Mendelian dominant. Identical twins have been found which show similar degrees of resistance whereas such close concordance is not seen in nonidentical twins.[3] The various inherited, environmental, pharmacological and technical factors thus combine to render adequate control of anticoagulatant therapy very difficult. Even in the Medical Research Council study where extreme care was taken in supervising anticoagulant therapy, nearly half of the values of the "thrombotest" were found to be outside the therapeutic range. The inadequacies of the control of anticoagulant therapy with coumarin drugs have undoubtedly contributed to the difficulties of assessing the clinical usefulness of these drugs.

Disappointments at the failure of oral anticoagulation therapy to influence greatly the mortality from occlusive vascular disease has led to the exploration of other modes of therapy. The recognition that the thrombus which forms in an artery is white, consists of platelet aggregrates and does not depend upon fibrin deposition has clarified why anticoagulatants have been ineffective. This has led to the exploration of other modes of treatment drugs which prevent platelet adhesiveness. A number of such drugs which inhibit platelet aggregation in vitro and can be given orally are now known i.e. aspirin, dipyridamole sulphinpyrazene. Dipyridamole has lately been reported to cause a decrease in the frequency of arterial thrombi in patients with prosthetic heart valves.[4]

Venous thrombosis has always been thought to be due to increased coagulability of the blood and reduction in blood flow. Early ambulation has overcome the latter factor and greatly reduced thromboembolism after surgery. The first factor has been thought to be controlled with heparin or anticoagulant drugs. In view of the disappointment with anticoagulation, a recent report compares the effectiveness of warfarin, aspirin, dipyridamole and dextran in protecting individuals from venous thromboembolism after arthroplasty of the hip.[5] Aspirin seemed to be fully as effective as warfarin and more so than dextran and dipyridamole. The explanation turned out to be that the venous thrombus also seems to start with a platelet nidus aggregate about which fibrin then precipitates to form the typical red thrombus. The conclusion reached was that by preventing the original platelet nidus aspirin served also to prevent the red thrombus.

The British Medical Research Council has been conducting a trial of aspirin in the prevention of leg vein thrombosis post-operative and its conclusion will be awaited with much interest. A controlled trial of sulphinpyrazone in doses sufficient to suppress platelet aggregation to a collagen stimulus has recently been completed in a group of elderly male patients and a significant improvement in mortality was seen in the treated group. Thus, some evidence has accumulated to suggest that inhibitions of platelet aggregation may prove to have a place in the management of thromboembolic disease. What we all hope for is continued extensive trials to continue with these agents in a variety of conditions so that we may be secure of this place in the therapeutic armamentarium.

The therapeutic value of the dicumarol group of drugs has been bedevilled by statistical, clinical and laboratory pitfalls that will be more easily avoided in the future assessment of the value of the antiplatelet drugs presently coming under close scrutiny.—L.H.N.

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Death Of A Human Being: Neocortical Death

Increasingly it is accepted that death of a human being means death of his brain, indeed his mind and nothing else. Early criteria were too stringent in that any reflex activity was regarded as incompatible with the definition of death of the brain since what was diagnosed in such circumstances was not death of the brain but global death of the whole central nervous system, brain, mid-brain and brain stem. In this situation if it were possible by mechanical respiration to avoid cardiac arrest or if spontaneous respiration persists in the presence of a dead neocortex, the individual would still be considered to be "alive."[1]

We are all confronted with particular situations after cardiac arrest or cerebral infarction where spontaneous respiration, coordinated movements, reflex activity at brain stem and spinal cord levels may return in occasional cases despite the persistence of an isoelectric EEG. In this situation the critical clinical question is whether consciousness and intellectual activity will or will not be restored. Brierley[2] reported two cases with death of the cortex only after cardiac arrest. One was unconscious for 5 months, was kept alive with tube feeding because there was eye opening, yawning, and associated movements of spontaneous respirations and certain brain stem and spinal cord reflexes.

In both cases, neurophysiological investigation led to the conclusion that the neocortex was dead while certain brain stem and spinal centers remained intact. This was subsequently confirmed by detailed neuropathological analysis. There was intravital autolysis and few recognizable cytological elements. In essence, it seems that a person who resumes spontaneous respiration after cardiac arrest or retains it after cerebral infarction yet exhibits an isoelectric EEG was regarded as "alive" and kept going in this unconscious state while another surviving the

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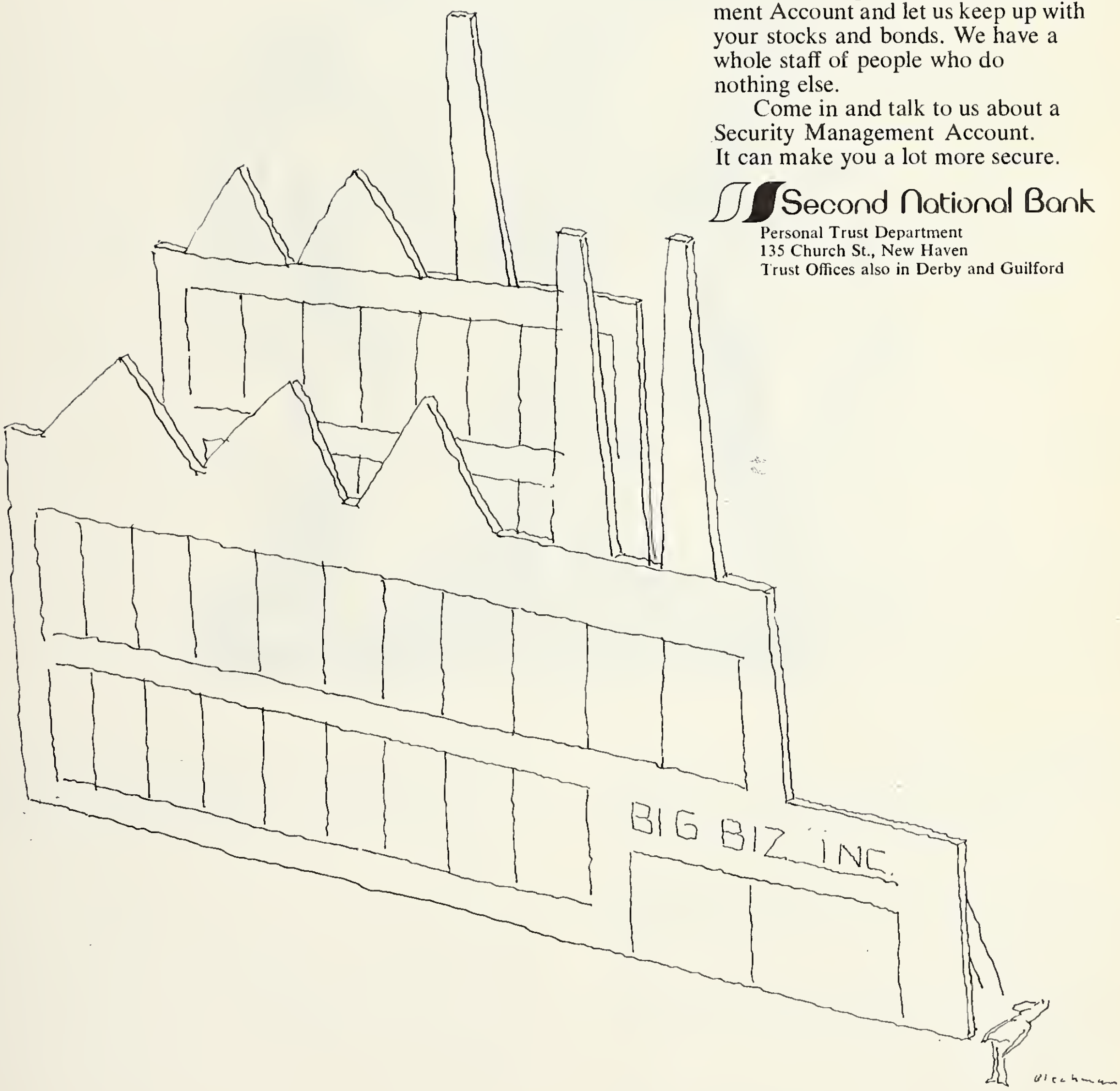

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Contraindications: Contraindicated in patients previously found hypersensitive to Trobicin. Not indicated for the treatment of syphilis.

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Warnings: Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance of *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia.

During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemo-

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Note: Antibiotics used in high doses for short periods of time to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Since the treatment of syphilis demands prolonged therapy with any effective antibiotic, and since Trobicin is not indicated in the treatment of syphilis, patients being treated for gonorrhea should be closely observed clinically. Monthly serological follow-up for at least 3 months should be instituted if the diagnosis of syphilis is suspected. Trobicin is contraindicated in patients previously found hypersensitive to it.

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*Data compiled from reports of 14 investigators. **Diagnosis was confirmed by cultural identitication of *N. gonorrhoeae* on Thayer-Martin media in all patients. Criteria for cure: negative culture after at least 2 days post-treatment in males and at least 7 days post-treatment in females. Any positive culture obtained post-treatment was considered evidence of treatment failure even though the follow-up period might have been less than the periods cited above under "criteria for cure" except when the investigator determined that reinfection through additional sexual contacts was likely. Such cases were judged to be reinfections rather than relapses or failures. These cases were regarded as non-evaluatable and were not included. JA72 1848-6

globin; hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25°C and use within 24 hours after reconstitution with diluent.
Male—single 2 gram dose (5 ml) intramuscularly. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.
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same accident also with an isoelectric EEG but whose cardiac function depends on mechanical ventilation may be regarded as "dead." Such a distinction between "alive" and "dead" attaches cardinal importance to the function of respiration and none to those higher functions of the nervous system that demarcates man from the lower primates and all other vertebrates and invertebrates.

Clearly when the neocortex is dead but certain lower centers remain functional this demands reappraisal of the definition of life and death. The Committee on Organ Transplantation of the Netherlands Red Cross Society[3] describes existing definitions and points out that there are criteria for defining "human" life but none for the definition of a "meaningful" life. The former demands an integration partly or wholly subserved by the brain function of the person himself. Brain death the Committee defines as irreversible loss of all brain function including the function of the brain stem. Obviously with the total and irreversible cessation of brain function the life of a human being has ceased. In the light of Brierley's observation, would it not be a significant step forward to say that if neocortical death is proved, the life of the human being has ceased to exist.

While such a view is not automatically acceptable as yet, it may be in the offing.

First of course, it must be generally agreed whether a state of cortical death can be diagnosed clinically. Then the distinction must be drawn between this diagnosis and irreversibility of serious brain damage or coma so that a decision can be made whether to cease efforts to prolong life. General guidelines can be drawn for diagnosing neocortical death but the other decision must be taken by each individual doctor on the spot. No one would disagree with the conclusion of the Netherlands Committee that the same criteria of death should apply to all human beings. If this can be established and be seen to be established whether to withhold further supportive measures or to pronounce the human being dead becomes an independent though crucial decision. It must be taken by a completely independent, experienced and numerically adequate group of doctors acting openly and with full knowledge not only of the patient's history and condition but of the attitude of close relatives, a suggestion made by the Netherlands executive committee.

This wise and human attitude provides a safeguard for anyone who has to make one of those onerous decisions. We may ask whether one of us would actually want his own vegetative existence to be artifically prolonged after the unequivocal diagnosis of neocortical death with permanent coma. Equally, who that knows the facts would want a close relative so supported. It is a dreadful decision but the answer can hardly be in doubt.

Brierley's documentation in clinical and neuropathological terms represent a challenge to any definition of life that is unconcerned with the functional and structural integrity of the neocortex.—L.H.N.

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Memorandum on organ transplantation presented by the Executive Committee of the Netherlands Red Cross Society. Third International Congress of the Transplantation Society, 1970.

Basic Science: Troponin-Tropomyosin

Even in the absence of extrinsic or neural control the heart is able to adapt very rapidly to changes in demand. One such adaptation is adjustment of cardiac output to alterations of venous return. From one beat to the next the heart responds to a change in the volume of blood returned to its chambers during diastole. A larger volume leads to increased force during the next systole: "The Starling Law of the heart."

The physiologic basis for this response is the slidingfilament hypothesis of muscular contraction. The stretching of the individual muscle fiber secondary to increased diastolic filling raises the number of tension developing bridges that can be formed between the sliding contractile protein elements actin and myosin and this mechanical rearrangement leads to augmentation of force during the next contraction. It is this intrinsic structural mechanism that enables the heart to adapt to changes in demand for volume.

What happens in the situation when the heart is called upon to develop greater tension and to develop it more rapidly without a change in the end-diastolic length of its cells. Bowditch in 1871 described the classic example of such an adaptation in the "staircase" phenomenon, a progressive increase in contractile tension developed by the heart upon an abrupt increase in contraction frequency. The increased tension is characterized also in an increase in velocity of tensions development such that more tension is developed over a shorter time as the frequency of the beating increased. This type of response develops without any change in diastolic tension or length and is therefore dependent on a mechanism clearly different from that upon which the Starling low is based.

Many aspects of the manner in which increased activation of tension developing bridges between actin and myosin are not yet clear but it is agreed that calcium ion has a crucial role in the process through its effect upon a rather newly discovered contractile protein troponin. It is now accepted that actin and myosin is inhibited by troponin which in association with tropomysin is attached to the actin filaments at regular intervals. For force to develop the inhibitory effect of troponin must be removed. The calcium ion is of critical importance in this respect. For as free calcium concentration rises above 10^{-7} M., it binds to an increasing number of troponin sites and removes the troponin inhibition of bridge formation between actin and myosin. During diastole free calcium concentration about the filament is below 10^{-7} M. The troponin tropomyosin complex blocks bridge formation and the muscle is fully relaxed.

Upon electrical excitation of the myocardial cell membrane calcium is released from storage sites probably at or near the surface, its free concentration rises above 10^{-7} M. about the myofilaments, troponin-tropomyosin inhibition is removed at some sites, bridges form and systole begins. Full activation of all available sites is achieved as calcium concentration increases to a value of approximately 5×10^{-6} M. or some 50 times the value of the relaxed state. It is apparent that tension and its rate of development can be modulated by control of the number of sites activated during systole and that the number of sites activated is proportional to the amount of calcium released upon excitation. Tension and its velocity will be graded from 0 to maximum at any given diastolic length as the calcium released is graded from 0-50 to 60 micro moles per kg.

Lanthanum, a trivalent cation completely eliminates tension but not the action potential, by binding the sarcolemmia and blocking calcium entry into the cell. Thus the basal membrane may be the site of superfical calcium binding and it is the calcium in the membrane which is in equilibrium with calcium in the interstitial space and accounts for the Bowditch phenomenon. An abrupt increase in the frequency of contraction causes an increase in the amount of calcium that influxes across the cell membrane to the myofilaments with each electrical excitation. This additional calcium binds to troponin sites and more completely inhibits the troponin-tropomyosin interference with actin-myosin coupling. In this way it produces an increase in tension and velocity typical of the Bowditch phenomenon. What we do not as yet know is why more calcium is induced to enter with each beat.

It is the depolarization of the myocardial membrane which permits calcium to enter the cell. If depolarization is prolonged calcium entry is prolonged. Increasing frequency of excitation shortens the action potential and the cell is depolarized for a shorter period of time during each excitation. This is readily recognized in the ECG. Movements of sodium are fundamental to the control of interrelated ionic processes. Decreased extra cellular sodium concentration is also associated with marked increase in tension and velocity and this correlates well with increased calcium influx.

With digitalis there is an increase in cellular sodium and increase in calcium influx and this could be the basis for the increased contractile tension produced by the glycoside in which there is also an increase in velocity of contractions. It thus appears that the ionic movements associated with the Bowditch phenomenon and those associated with digitalis administration seem to be quite similar. In both cases, there is an increased cellular sodium that leads to augmented calcium influx and thereby a positive inotropism.

If calcium binds troponin and thus releases the contractile mechanism, to achieve relaxation, calcium must be sequestered by the sarcoplasmic reticulum the energy source for the ATP and its hydrolysis is regulated by a separate ATPase from that required by the sodium pump. The amount of energy required to separate calcium from troponin is about 15 percent of the total energy output that is directed to relaxation. The cost of sodium pump transport is much less, approximately 2 percent of the total energy output.

Apparently a system in which the sodium ion is given a central role in the excitation contraction coupling helps to reconcile the studies focusing on active transport, ionic exchange, mechanical function, and electrophysiologic characteristics of the myocardium. The discovery of troponin, its binding to actin and its uncoupling by calcium to allow contraction has brought us a long way forward in understanding how the heart adapts very rapidly to changes in demand. —L.H.N.

Sudden Deafness: A New Concept In Salvaging Dead Ears

Until now half of the cases of sudden neurosensory deafness have been ascribed to Meniere's disease, viral infections or vascular lesions. Half have been labeled "cause unknown". Recent reports suggest that many cases of profound or total sudden hearing loss can probably be explained on the basis of mechanical damage to inner ear membranes—the round or oval window membrane. This recent hypothesis provides a reasonably satisfying explanation of such cases. If this hypothesis is verified it has implications for the treatment of sudden deafness by bed rest and if ineffective to surgical exploration of the ears as well as what activities may be permitted to patients who have suddenly developed dead ears.

In April, 1968, *Archives of Otolaryngology*, Dr. F. Blair Simmons described 15 patients with sudden, severe, sensori-neural loss, usually unilateral and associated with tinnitus. Each patient could document when he lost his hearing. Each had previously had normal hearing in the affected ear. Four patients lost their hearing in association with excessive alcohol intake, 2 on arising in the morning, 3 became deaf while driving an automobile. Seven recovered their normal hearing spontaneously, three within a week.

On the basis of these 15 patients and laboratory studies in experimental animals showing that intense sound can cause temporary breaks in Reissner's membrane (in the cochlear duct) Simmons advanced the theory of mechanical damage to the inner ear membranes as a hitherto unidentified independent cause of hearing loss. He also suggested three factors that may contribute to the occurrence of the intracochlear membrane ruptures: physical activity such as the valsalva maneuver that exceeds intrathoracic pressure and delivers pressure through the Eustachian tube into the middle ear. Another method could be extracranial venous or cerebrospinal fluid pressure and lastly, drinking too much alcohol.

Verification of this hypotheses was last to appear. Dr. G. A. Fee of Canada, described three cases of neurosensory hearing loss, dizziness and other variable symptoms following head injuries. He carried out tympanotomy in each patient and found perilymph leaking from the oval window into the middle ear. The patient's hearing partially resolved by surgical correction of the oval window fistula. Those are the first cases of surgery performed on the oval window for sudden, profound deafness.

Another report by Stroud and Calcaterra described spontaneous perilymph fistulas involving the oval window that occurred in three patients during moments of increased intracranial pressure such as bending over, laughing and singing. They explored the middle ear to close the window with gelfoam or adipose tissue.

Dr. Goodhill presented 4 cases of fairly sudden hearing loss, and explored the middle ear by tympanotomies of three of these patients. He demonstrated perilymph leakage into the middle ear from the oval or round window or both. A fourth patient was a 40 year old man who had made a shallow scuba dive and on ascent noted a "pop" in his right ear accompanied by tinnitus but no vertigo. Ten days later he was placed on absolute bed rest and intravenous procaine. His hearing returned to normal three days later.

The loss of hearing in the first three patients involved different types of physical exertion. One noticed a "pop", total deafness in the left ear and roaring tinnitus after doing 47 sit-ups. Eventually he also experienced severe vertigo and vomiting. A second patient awakened with almost total left hearing loss and roaring tinnitus after an excitable alcoholic New Year's Eve. The third developed it while cheering and rooting at a football game. No other cause beside physical exertion could be found. When the rupture of the round and oval window in two patients was closed surgically the hearing returned dramatically. The third came months after the injury and did not recover his hearing.

When there is no spontaneous recovery or viral and vascular or ototoxic drugs involved, exploratory tympanotomy and careful search for an oval or round window rupture is indicated.

This seems to be the only way to diagnose such a condition at present.

The concept offers a new approach to salvaging dead ears.—L.H.N.

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More On Atmospheric Lead Pollution

A special committee of the National Research Council was appointed to study and report on the biological effects of atmospheric pollutants to clarify the effect of this health hazard. Based on an extensive survey of the literature on lead pollution, the study comes up with the finding that the concentration of lead in the largest cities in the U.S. is 20 times greater than over the sparsely populated rural areas and more than 2,000 times greater than in the air over the center of the Pacific Ocean. There is no doubt that man has substantially contaminated some parts of his environment with lead. It is also clear that one major source of general contamination is the combustion engine and dispersal of lead allyl compounds used as automotive fuel additives.

There has been little change in the average content in the air over the major American cities over the past 15 years. Accordingly, the panel expects little further change in the magnitude of the effect on biological systems for some years to come. A more important source of lead in the blood appears to come from food and drink. In any case, the average city dweller in the U.S. receives insufficient doses of lead from both the air he breathes and the food he eats to pose a threat to his health. However, running through the report is the assumption that blood levels below 40 micrograms per 100g of blood are not biologically harmful because it is only above that level that synthesis of the heme part of the hemoglobin molecules is affected and the first clinical symptoms of lead poisoning (mild anemia, headache and generalized muscle aches) are not *noted until blood levels* exceed about 80 micrograms per 100g whole blood.

The panel report cites studies which show that the average person living and working in the city of Los Angeles, where the concentration of lead in the air is twice as high as in most other cities, will have a blood lead content of less than 25 micrograms per 100 gr. of whole blood and inhabitants of other cities are likely to have about 15 micrograms. On the other hand children who live in larger cities and some groups of workers such as policemen and parking lot attendants are at a high risk from airborne lead which may result in blood level concentrations greater than 40 micrograms per 100g of blood. In some of these, very high levels of lead in the blood are readily sufficient to produce clinical lead poisoning.

The exposure of city children to airborne lead and also to lead paint and other sources is a much more intractable problems. For one thing, recent studies have shown that many city children have blood lead concentrations of 40-60 micrograms per 100g blood. Leaving aside the ingestion of paint which is a major problem in the poorer sections, the panel points out that children living in large cities are also exposed to high risk of lead poisoning through dust and grit in the streets. Such dust often contains more than 2,000 micrograms of lead per gram, and if a child manages to eat only about 40 milligrams per dust each day, his blood lead content could be taken above the 40 microgram level. If he ate more than 0.4 gram of dust per day, he would show symptoms of clinical lead poisoning even resulting in damage to the C.N.S. This, says the panel, is an undesirable level of exposure. Unfortunately, no one presently knows how much dust and grit is swallowed or inhaled by children in large cities. Such a study is urgently needed.

Will such findings of blood lead concentrations lead to a ban on lead in petroleum? On strict biological grounds, the panel's clinician, Dr. Paul B. Hammond said that a case could be made out for banning lead in gasoline, but he went on to say that one could make out a case also for banning the auto as a lethal weapon on the same grounds. Unfortunately, economics enter the picture here. However, it may turn out that the auto manufacturers themselves will be forced to conclude that they can no longer afford to have their cars run on leaded petroleum. By 1975, they must meet strict regulations on the amount of unburnt gases and nitrogen oxides emitted from auto exhausts. One method which at present looks promising is to attach a catalyst to the exhaust system to reduce nitric oxide and to oxidize C.O. Lead, however, poisons the catalyst.

Apart from its findings on the levels of lead in the blood of city dwellers, the panel also pinpointed areas where more research is needed. For one thing, present monitoring of both city air and food is totally inadequate to determine either the source of lead which eventually finds its way into human blood or to provide warning of potential risk. But the chief areas where more extensive research is called for be in the biological sciences themselves. For example, the panel says that studies are required to determine whether the body burden of lead increases with age and the assumption that the non-diffusable fraction is tightly bound in bone and therefore biologically inert, also requires further detailed examination.

It must be emphasized that our knowledge of the effects of blood lead levels below 40 micrograms is not known and studies are urgently needed on the biological effects of low levels of exposure to lead. The subtle effects on behavior of low lead exposure of long duration may be manifest in two types of disorders, the dulling of mentation and chronic hyperkinesis. No information is available regarding the possibility of cause and effect in what may be an extremely important problem. The effect of low lead exposure of long duration on the aging process and on resistance to infection is also unknown. Accordingly, the panel's assumption that 40 micrograms of lead per 100g blood is safe, must be taken with reserve.—L.H.N.

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Myocardial Revascularization

Long range studies have provided the natural history of patients with angina pectoris and of those who have suffered a myocardial infarction. In a well controlled study of 2,234 soldiers followed for 15 years, Zukel et al[1] showed that about 3 percent of patients with angina die each year with present conservative treatment. However there are several types of patients that urgently require more than conservative medical management. One is the disabled angina pectoris patient who is unresponsive to therapy. Another is the patient with an impending myocardial infarct. These two conditions have a high risk under medical management.

Years ago The Vineberg procedure of implanting the mammary arteries into the myocardium was offered as a relatively benign surgical procedure to revascularize the myocardium. With its improvement so that, both the anterior and posterior regions of the left ventricle can be vascularized, the operation is still performed whenever the three coronary arteries are seriously affected and cannot be bypassed by an aorta-venous graft. The present tendency among cardiologists is to offer a patient with angina pectoris an aorta-coronary vein bypass to revascularize the myocardium when feasible. This means that there must be a run-off piece of coronary artery beyond an obstruction to which the graft can be sewed.

This operation is being enthusiastically received by many cardiologists as a major breakthrough in the conquest of our number one killer. However, there remains much skepticism by others because after 20,000 such operations in the last year we do not even know the first fact —namely whether vein bypass increases survival. Nor have there been established indications, contra-indications and constraints for the new vascularization procedure. By appearing to lessen angina the operation might improve the quality of life. However, the patient must first survive the operation.

We know that the immediate mortality even in uncomplicated cases without advanced damage to the left ventricle can be up to 10 to 15 percent. We know grafts begin to show the first stages of atherosclerosis within months after implantation. We know that one year after revascularization about 22 percent of vein grafts are occluded. Cardiac function is worsened in 50 percent of those with previous myocardial damage and 18 percent of patients have sustained a new myocardial infarct.[1]

By comparing these figures with the figures of Zukel on the natural history of patients with angina, revascularization procedures will have a hard time competing with them because to start with the data thus far indicate a national mortality of 10 percent for the operation alone not to speak of the morbidity after survival. The operation, of course, is not easily resisted in patients whose life is intolerable with intractable angina or insecure in a patient with impending myocardial infarction. But even in patients with cardiogenic shock only 27 percent of patients were saved by emergency revascularization, not much of an improvement when compared with medical means of treating such patients. Revascularization is being advised for the control of unresponsive arrhythmias and for patients in whom progressive extension of the area of ischemia has occurred a few days after the initial occlusion.

At the present time it would appear that revascularization procedures should not be performed in the asymptomatic coronary patient because of the high rate of vein graft obstruction and by comparison with the natural course of events in such patients under medical management which carries a mortality of only 2-5 percent. When sufficient experience is obtained through a cooperative registry in which patients are studied over a 3-5 year post-revascularization period, will we learn if revascularization offers any benefit over medical management. Only then will we be able to determine if surgery should be performed on patients such as those with mild drug responsive angina pectoris or on the asymptomatic patient following myocardial infarction who has a specific lesion such as the allegedly dangerous chronic left anterior descending artery occlusion.

It is not going to be easy to evaluate the clinical benefits in surviving post-revascularization patients. Coronary arteriography which demonstrates whether the bypass is patent does not measure the degree of blood flow. The ECG cannot be used as a reliable index of improvement because it often remain abnormal after the operation and an inverted T which becomes upright after exercise does not mean improvement in function. Dramatic relief has been reported in 60-90 percent of anginal patients surviving. Unfortunately, the decrease of pain cannot be used as a guide because it has been shown that after a sham operation of only skin-cutting there occurred a significant relief of angina in 60-70 percent and that a placebo can give relief to anginal symptoms in 60 percent.

Corday[1] urges that proper studies be instituted in order that the profession may learn if it is worthwhile before revascularization procedures become established as a standard practice. Once procedures are established they become routine and it takes a long time to overcome preconceptions.[3] Fifty years after the acceptance of radical breast surgery, investigators are just beginning to question whether simple surgery with radiation might not be a more effective and less mutilating procedure.

What we should have is a national body to take on the responsibility of a registry of all cases for cooperative study based on survival, clinical progress, roentgenography of the heart, visualization of the coronary circulation, stress testing, existence of arrhythmias, cardiac decompensation and other complications. Post-operative angiographic studies should be compared with the preoperative findings in order to determine if some lesions are of more significance than others. Each lesion must be classified as to the location, degree of arterial obstruction, degree of heart damage and cardiac decompensation. Then we should have a clearer picture of the type of care likely to benefit a coronary patient compared with the risks involved in surgery.—L.H.N.

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Psychiatric Insights Of Zen

In most cultures there was a belief in the divine origin of the healing art. Christ's leadership is still a potent influence in western medical thought and practice. This is also true of orthodox Jewish religion, in which thrice daily in his prayers the devotee praises the Lord with the title "The healer of the sick." On the whole the belief in the divine ancestory of medicine has left but vestigial remnants. In the case of Buddhism, however, there is a direct link between, the original religious superstructure and an existing therapeutic method—known as Zen Buddhism.

This kind of Buddhism is a kind of religious meditation, a means of achieving ultimate truth, but also an end in itself. Zen does not rely on texts on scriptures but rather transmits teaching from mind to mind from a master directly to his disciple without the intervention of rational argumentation or formulation in conceptual terms. Above all, Zen is a religious discipline that requires complete submission to the will of the Master who alone can guide authoritatively and ensure the correct transmission of the truth. Zen teaches that Buddha-nature is inherent in all human beings and can be seen through meditative introspection. The great Zen masters advocated "absence of thought" in order to free the mind from the bonds of the external world. They also taught the need to ignore one's feelings which is the essential element in the psychotherapy that has evolved from the doctrine.

There are two basic tenets of Zen Buddhism. One is the importance of nature and life in and with nature. Second the immersion of the individual in the family, in the group and the community. For the practice of proper conduct according to these beliefs, Zen monasteries constituted a focal point. Life here counteracted alienation from nature and society. Such a situation was enough to attract not only the devout but also numerous mentally disturbed people who sought refuge. To all comers, healthy or disturbed they applied the same treatment, insistence upon strict conformity with rules of Zen conduct. The results were often surprisingly fortunate.

This led a Japanese physician, Shomei Morita of Jikei University to undertake a mode of therapy with neurotic patients that has no correlate or parallel in the Western world. The first major element was to combat the egocentricity which is a most striking symptom of a patient's neurosis. The second element in Morita's therapy is the correction of the patient's alienation from nature. Dependence upon and love of nature characterizes the Japanese in physical and emotional health. There are now ten Morita treatment centers in Japan in addition to that of Jikei Medical College in Tokyo. In all of them the therapy aims to restore love of nature and abolish egocentricity. Both of these major emotional adjustments can be achieved only with the iron discipline that is practiced in Zen communities.

Morita's therapy follows a specific schedule or ritual on which recovery is said to depend. On arrival at the hospital, the neurotic patient—overt psychotics are not accepted—must have complete bed rest for as long as a week. During this time he is not permitted to associate with any one else. He must not read, smoke, telephone or watch television. He is left alone with his illness until he and his illness become one. He has to accept his illness in complete solitude.

This initial period of absolute isolation and immobility in bed is by far the most traumatic phase of Morita's therapy. In this phase the therapy is somewhat reminiscent of S. Weir Mitchell's famed "Rest Cure." Subsequently, the patient is gradually restored to the world. He is encouraged to engage in work in a garden surrounding the hospital. This activity is intended to encourage the patient's emotional return to nature. Gradually also the patient is permitted renewed contact with other persons. Rather late, he also meets with the therapist not in the intimate setting of a doctor's office but on a walk through the garden, or during a game of table tennis or during a similar diversion. In short, there is no occasion or indeed encouragement for the patient to bare his own soul because that would only serve to reinforce the egocentricity which is assumed to be the essence of his neurosis.

Furthermore, in a subsequent stage of therapy when the patient is given the task of keeping a diary he is enjoined to refrain from recording anything that relates to his emotions or to his illness. The physician who checks the daily entries, somewhat in the manner of a severe teacher, applauds the patient if he is able gradually to free himself from the hypochondriacal self-importance that held him in bonds. In fact, it is the physician's explicit task to induce the patient to become once more a part of society from which he had been alienated. The patient must learn to associate with his fellowmen without friction and to perform his work as best he can even by the standards of a healthy society. He must never in the course of his treatment be permitted to think of himself as an emotional invalid or as different from the rest of the community.

It is clear that this tightly scheduled mode of therapy, a rigid form of re-education is an outgrowth of a basically different concept of health and disorder, than that underlying Western therapy which is derived from concepts as psychic, spirit or soul. On Zen thinking, the rules are rigid and immutable. That is why it was possible to integrate them in a psychotherapeutic system such as that of Morita's therapy. It is, however, strange that even though this type of philosophy so closely approximates Japanese beliefs that only ten institutes have thus far flourished in Japan. It will be interesting to learn how successful Zen Buddhism is in combating neurotic illness as compared to our own. Especially whether our philosophy of life will allow success by this method in the Western world.—L.H.N.

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Dissolving Gallstones In Vivo

In this country over 15 million people have gallstones and one-third are removed by operation. The total expense of this one disease is approximately one billion dollars.[1] Medical therapy would certainly represent a major advance in the treatment of one of the most prevalent diseases of Western Civilization. However, like any new approach to the solution of a medical problem we depend upon basic research to point the way. One major contribution was the observations of Vlahcevic[2] that patients with cholesterol cholelithiasis have a diminished bile acid pool and a diminished bile acid secretion rather than an increased cholesterol secretion.

If this were true then expansion of the bile acid pool by bile acid feeding should increase the secretion of both bile acid and lecithin. Since bile salts and especially bile salts and licithin can be used to dissolve gallstones in vitro[3] it seemed reasonable to attempt to modify hepatic secretion to create a type of bile that would favor dissolution of gallstones in vivo. Thistle and Schoenfield were able to improve the ability of bile to solubilize cholesterol in vivo by feeding chenodeoxycholic acid (CDCA) to patients with gallstone disease.[4,5] At a daily dose of 0.75 to 1 gram of CDCA, cholesterol crystals disappeared from bile but stone dissolution was not documented over a 4 month period.

Danzinger[6] now reports evidence for actual dissolution of gallstones in 4 out of 7 patients using higher doses to CDCA up to 4.5 gr. daily and for longer periods of time. The women were incapable of childbearing who had functioning gallbladders with asymptomatic radiolucent calculi. In one case three small gallstones disappeared after six months. In a second case, a single large calculus progressively diminished over 22 months. In a third case, multiple calculi progressively decreased from 10-3.5 mm. over a period of 18 months. In a fourth case, multiple calculi with a mean diameter of 11 mm. were reduced in number and the remaining stones decreased in size to a mean diameter of 8 mm. The biliary bile acid composition changed to become more than 90 percent chenodeoxycholic acid.

The probability of the spontaneous dissolution in these patients seems remote since gallstones had remained unchanged for a period of 5½ years and 4 months respectively. The bile acid pool size now recognized to be decreased in patients with cholesterol cholelithiasis was expanded markedly with chenodeoxycholic acid and the bile composition improved. Of course, a gallbladder that can accept and expel bile is essential to ensure the continual bathing of gallstones with unsaturated bile. If unsaturated hepatic bile enters the gallbladder and rapidly took up cholesterol from stones until it became saturated with cholesterol then the stones should dissolve in a few weeks. This did not occur in Danzinger's cases indicating that dissolution occurred at a limited rate.

These findings are, of course, preliminary and deal with a small group of patients. Nevertheless, the results are exciting and provocative. The first question that arises is how safe is prolonged therapy with chenodeoxycholic acid. The only symptomatic complication with this bile acid was diarrhea which was readily controlled by reduction of dosage. Mild but transient elevation of SGOT and alkaline phosphatase were seen in several of the patients but liver biopsies were all normal at 6-12 months.

The bile acid is converted by colonic bacteria to lithocholic acid which is a potent hepatotoxin when fed to animals. However, lithocholic acid concentration increased only slightly in bile and this suggests that little was absorbed from the colon in these patients. A help to prevent lithocholic acid production is to administer chenodeoxycholic acid in unconjugated form which makes it readily absorbed from the jejunum as well as being insoluble at gastric pH thereby rendering it inactive against gastric mucosa.

One question is what happens to cholesterol metabolism. We know that bile acid feeding suppresses endogenous bile acid synthesis in man and since serum cholesterol levels did not rise in the reported cases, synthesis of cholesterol may also be inhibited. But we need further studies of cholesterol metabolism. The effect of chenodeoxycholic acid on other disorders such as hyperlipidemic states and intestinal or liver disease is unknown.

Chenodeoxycholic acid cannot be isolated conveniently from animal bile and must be prepared synthetically. At present its cost is moderate. However, its price could fall considerably if methods for its synthesis were improved.

The position at present is that we are presented with a possibility—of a novel and exciting form of medical treatment for cholesterol gallstones. Long term clinical trials to examine the effectiveness, indications for, and safety of chenodeoxycholic therapy are now in order. If the method proves successful, operation on gallstones may become as outmoded as operation on mastoid.—L.H.N.

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Lesions In Saphenous Vein Bypass Grafts

(*Circulation*, 44: 719, 1971, Vlodaver, Z. and Edwards, J. E.) Saphenous vein tissue is commonly used in constructing bypasses between the aorta and a coronary artery around an occlusion. Now a few reports of the development of fibrous intimal thickening in the bypass vessels have appeared.

Nineteen grafts in place less than 8 days showed no lesions. Two grafts that had been in place for a month showed lesions consisting of minimal fibrous thickening of the intima. This seemed to represent the earliest stages of the lesions that were found to have developed in the 8 specimens obtained 3½ to 9 months after the operation.

The fibrous thickening was characterized by an increase in fibroblasts lying in a mucoid matrix. Foam cells surrounded the lumen. Fat stains revealed no fat in the foam cells. The mucoid matrix gave a strongly positive test for mucopolysaccharides. Two of the grafts had thrombi apparently related to atherosclerosis adjacent to the graft.

The findings show that non-lipid lesions basically fibrous and mucopolysaccharide in nature develop during the early stages of atherosclerosis even in those patients in whom the more advanced atherosclerotic lesions have become established.—L.H.N.

Cardiac Arrest In Patients Without Myocardial Infarction

(*Circulation*, 44: 688, 1971, Camarata, S. J., et al) studied 193 episodes of cardiac standstill in 132 patients. Forty-five had a second episode and 16 a third. Regardless of which episode was involved, the immediate recovery rate was approximately 40 percent. However, the long term survival was negligible. Only five patients who had one episode and one who had had two, survived.

Sixty-five of the total series had respiratory acidosis due to pulmonary disease or drug overdose, 34 with metabolic acidosis due to hemorrhagic or septic shock and 30 with some iatrogenic disease such as reaction to medication or inadequacy of airway manipulation. No patient survived with acidosis caused by progressive cardiac or respiratory failure.

It is interesting that of 20 patients who developed cardiac arrest due to medication, twelve had received aminophylline into the right atrium through a central venous catheter in a dose of 250-750 mg. given in 3-5 minutes.

If we omit the cases due to iatrogenic disasters the lifesaving results of this procedure are nil.

—L.H.N.

The Syniatrist

(*JAMA*: 217, 1971, Silver, Henry K.) Dr. Silver to clarify terminology describing health professionals, recommends the term syniatrist—an individual practicing in association union or together with a physician.

It would apply only to health workers who have direct contact with patients in providing health care under a physician's supervision.

He proposes 2 principle subdivisions: the area of the specialty of practice and the relationship of syniatrist to the physician. Several terms are offered:

(a) General practice syniatrist associate.
(b) General practice syniatrist assistant.
(c) Pediatric syniatrist associate.
(d) Orthopedic syniatrist assistant.

These would depend on the level of training, competence, and independence of judgment, decision making and accountability required of the syniatrist.–L.H.N.

Special Article

Incorporating Your Practice—A Practical Guide

David P. Simerman, Attorney-at-Law

One of my closest friends, a successful orthopedist, tells of an incident which occurred during the lean years of his internship at a prestigious New York hospital. My friend was replenishing his usually depleted bank account, when he happened to meet the head of his Department at the bank. This Doctor, both professionally and financially one of the leaders of his profession, wondered in jest where this young intern was accumulating enough money to put in a bank. When my friend answered "It isn't easy", the response was "It never will be".

And it isn't. Despite some relief brought by the Tax Reform Act of 1969 (referred to by some as the Accountants and Lawyers Relief Act), after taxes are paid, and after one's children are educated, there is often precious little left, even from a successful physician's earnings, to provide the basis for an adequate retirement income. Frequently, practice in corporate form provides at least a partial answer to this problem, and as a result, more and more physicians and other professional people are incorporating their practices. This article will discuss some of the financial and tax advantages of corporate practice, and some of the day to day practical requirements of operating a professional corporation.

I. The Financial and Tax Benefits of Corporate Practice

All of us who have ever taken a basic course in economics have learned that a corporation is defined as "an artificial person or legal entity created by or under the authority of the laws of a state . . . which is regarded in law as having a personality and existence distinct from that of its several members . . ." (Black's Law Dictionary, Fourth Edition, 1957). The concept of the artificial person, being a separate entity, is crucial in understanding the distinction between practicing as an individual or as a partner, and practicing under the umbrella of the professional corporation. The individual and the partner are self-employed persons. There is no distinction drawn between the income of their practices and their personal income. They are one and the same, and for tax purposes are reported as one and the same. By contrast, when Dr. John Doe incorporates his practice, it is no longer John Doe, M.D. who holds himself out as offering medical services to the public—it is *John Doe, M.D., Professional Corporation,* a separate entity by whom Dr. Doe is employed. John Doe, M.D., Professional Corporation, files a corporate income tax return, and Dr. John Doe files an individual income tax return reflecting his earnings as a corporate employee. Perhaps a fine distinction, but as we will see, a critical one—for by the mere act of filing a certificate of incorporation Dr. Doe has become eligible for a whole grab bag of money-saving benefits unavailable to him as an individual practitioner, i.e. a "qualified" pension or profit sharing plan, medical and disability insurance benefits, medical payment benefits, and tax deductible life insurance.

A. *The Qualified Pension or Profit Sharing Plan*

Basically the purpose of a pension or profit sharing plan is to allow the participant in such plan (the individual professional) to accumulate income free of tax as a nest egg for his retirement. Amounts contributed to a pension or profit sharing plan by an employer (the professional corporation) are tax deductible by the employer when contributed but are not taxed to the employee at that time. When these contributions are placed in trust for the benefit of the pension or profit sharing plan participants, the funds may be invested in stocks, bonds, real estate or any other investment media suitable for trust funds, and any income realized by the trust is likewise allowed to accumulate tax free. All payment of tax is deferred until benefits are actually paid to the employee from the pension or

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profit sharing plan trust. At that point, if benefits are paid in a lump sum, the amounts representing the actual contributions made to the employee's account are taxable at ordinary income rates to the employee, but all income and all capital appreciation on these amounts are taxable to the employee at the lower capital gains rate. Lump sum pension and profit sharing plan benefits under the present Internal Revenue Code qualify for seven-year income averaging, thereby reducing the tax rate on these benefits. Further, the plan may provide for benefits to be paid not as a lump sum, but as an annuity—for the life of the retired participant, or for the life of his beneficiary. Annuities are taxable under special I.R.S. rules. However, the effective tax rate is generally relatively low, since the annuity is received during the employee's retirement years, when his income is, in most cases, substantially lower than during his employment years.

A pension plan is a type of plan which imposes a fixed annual liability upon the business. There are two types of pension plans. First is the money purchase plan, which provides for a contribution based upon a fixed percentage of compensation. The ultimate accumulated benefit depends upon earnings and years to retirement. For instance, if a person age 35 earned $60,000 a year to retirement and a contribution of 25% of compensation were made every year, (the maximum generally allowed under I.R.S. rules) the amount of the fund accumulated to age 65 (assuming 5% interest earned on the fund) would be $996,570. Chart #1 shows accumulation for other ages and salary levels.

Second is the fixed benefit plan. In this type of plan, the ultimate pension benefit is predetermined and the required annual contribution to produce the benefit is actuarily determined. Fixed benefit plans are not subject to the 25% limitation of the money purchase plans. Therefore, much greater amounts can be accumulated. However, this virtue is offset by the lesser flexibility of the fixed benefit plan.

CHART 1

MONEY PURCHASE PENSION PLAN

Age	*Compensation*	*Annual Contribution to Pension Plan**	*Lump Sum Amount Available At Age 65***	*Monthly Pension If Paid Out Over a 20 Year Period***
35	60,000	15,000	$ 996,570	$ 6,663
35	80,000	20,000	1,328,760	8,884
35	100,000	25,000	1,660,950	11,105
45	60,000	15,000	495,975	3,316
45	80,000	20,000	661,300	4,421
45	100,000	25,000	826,625	5,527
55	60,000	15,000	188,655	1,261
55	80,000	20,000	251,540	1,682
55	100,000	25,000	314,425	2,102

* Maximum allowable contribution is 25% of compensation.
** Assumes 5% interest earnings compounded annually.

The profit sharing plan is somewhat similar to the money purchase pension plan in that the contribution is expressed as a percentage of compensation. However, the profit sharing plan is more flexible in that no fixed annual liability is imposed on the corporation. Contributions can only be made out of profits, and then may be made at the discretion of the directors. The maximum contribution for which the employer may obtain a deduction is 15% of compensation.

Retirement plans in general may provide for additional ancillary benefits such as early retirement, disability retirement, death benefits including widows benefits, and vested benefits on termination of employment. In addition, a retirement plan can provide for voluntary contributions made by the individual participant in addition to contributions made by the employer which enable the participant to contribute after tax dollars and defer payment of tax on the earnings of such contributions until actual receipt. A retirement plan may also provide for a death benefit. If someone other than the estate of the employee is designated as the beneficiary, the death benefit will not be includible in the taxable estate of the employee.

The availability of the qualified pension or profit sharing plan is perhaps the greatest single inducement to incorporation. Under the Internal Revenue Code these plans are available only to corporations. By contrast, unincorporated businesses have available only the limited benefits of the HR-10 or "Keogh" type plans, where the maximum annual deduction with respect to a pension plan contribution for the benefit of an owner or employee is 10% of that owner or employee's annual compensation, up to a maximum allowable deduction for any individual of $2,500. As can be determined by simple arithmetic, any professional earning in excess of $25,000 annually fares better, for retirement plan purposes, under the corporate, qualified pension or profit sharing plan.

Although the qualified plans have tremendous potential for the accumulation of wealth, the Internal Revenue Code does exact a price. In order for a pension or profit sharing plan to qualify for the favorable tax treatment discussed, it must cover not only the professional employees of the corporation but nonprofessionals as well, such as nurses and secretaries. This is not as onorous a requirement a might appear, however. First, the Internal Revenue Code permits a reasonable waiting period to be imposed before employees are eligible to participate in the plan. Generally, waiting periods of two years have been accepted by the Internal Revenue Service. As a result "high turnover" employees can be excluded from coverage. Further, the Service permits gradual "vesting" of benefits.

Under provisions for gradual vesting an employee does not become entitled to a full pension benefit unless he has been a participant in the plan for a specified period of time, e.g. ten years. If his employment terminates before this time, he is entitled only to a proportionate share of the pension benefit. The plan might provide, for example, that an employee's entitlement to a pension benefit "vests" to the extent of 10% for each year he is a participant in the plan. If he leaves after his first year of participation, he is entitled at retirement age to 10% of the normal benefits under the plan; if after his second year, 20%, and so on. The plan might provide as well that any portion of a participant's account in a retirement plan trust which consists of employer contributions, (and the income thereon), and which is not vested, may be deemed forfeited, and under certain conditions redistributed to the accounts of other participants in the plan (including stockholders and other professional employees). Forfeitures can also be applied so as to reduce the contributions which the professional corporation must make to the plan in future years.

B. *Medical Insurance, Medical Payments, and Disability Insurance*

The incorporated professional has additional tax savings opportunities by virtue of the broader deductions available to the corporation for medical insurance premiums and for payment of non-insured medical expenses. Again, this broader deductibility results from the theoretical difference between the individual practitioner and the partner, on the one hand (the self-employed professional); and the incorporated professional on the other (the employee). Under the Internal Revenue Code, medical insurance premiums paid by a business for the benefit of its employees are fully deductible as a business expense but are not taxable to the employee. Thus when an individual practitioner or partner pays the premium on group insurance coverage for his employees, that premium is deductible as a business expense. However, that portion of the premium attributable to coverage for "the boss" is not considered a valid business expense since "the boss" is not an employee. His tax deduction is therefore limited to the maximum permitted to individuals as a medical expense deduction on Schedule A of Form 1040. By the same token, when the professional corporation pays medical insurance premiums for its employees, the professional man is a bona fide employee, and that portion of the premium attributable to his coverage is fully deductible as a business expense of the corporation. Moreover, the corporation, to qualify for this deduction, need not cover all of its employees, but may elect to cover only a portion of them—even if coverage is limited to its sole stockholder employee. Additional benefits are available if the corporation elects to pay non-insured medical and dental expenses incurred by its employees. The corporation may pay these expenses for the benefit of all its employees; or may limit these benefits to only a few employees, e.g. its stockholder employees, and deduct all expenses paid as a business expense. The employees covered by these programs need not declare these payments as income. The practical result is that the incorporated professional's medical expenses become *fully* deductible, without that deduction being reduced by 3% of his adjusted gross income.

Similarly, all expenses incurred by the corporation for disability insurance premiums covering all or some of its employees, are fully deductible by the corporation as business expenses.

C. *Life Insurance*

Numerous opportunities for tax deductible, and low-cost life insurance present themselves to the incorporated professional. In an individual practice or partnership situation, life insurance expenses of the individual or partner are personal, non-deductible expenses. In a corporate situation, however, the corporation may purchase term life insurance payable upon the death of an employee to that employee's designated beneficiary. Premiums paid on the first $50,000 of term life insurance are deductible by the corporation as a business expense, but are not taxable to the employee covered. As a result, the incorporated professional can acquire his first $50,000 of life insurance with pre-tax rather than after tax income.

Additional opportunities for the corporate professional to acquire low cost insurance are available through the split dollar insurance device. Under this arrangement the corporation owns the cash surrender value portion of the policy, and the employee owns the insurance portion. By the same token the corporation pays that portion of the annual premium representing the increase in cash surrender value, and the employee pays that portion of the premium attributable to the insurance portion. With each year that the policy is in effect, the cash surrender value of the policy increases, as does the corporation's share of the premium. Although the corporation incurs an expense represented by the increase in premiums, the increase in the cash surrender value of the policy (a corporate asset) offsets this increased expense. As the corporate asset increases, so does the value of the stockholder-employee's interest in the corporation. Similarly, with each year the policy is in effect, the employee's share of the premium decreases, frequently to zero after the policy has been in effect for three or four years. As a practical matter, under such an arrangement the employee's share of the premium buys substantially more insurance coverage than is available under even the most favorable term insurance policy.

Since the split dollar arrangement results in a financial benefit to the stockholder-employee, the value of that benefit is taxed to the employee as income. The value of the benefit is deemed to be the Internal Revenue Service's designated value of the amount of term insurance covering the employee under the plan, less the actual premiums paid by the employee.

II. Practicing As A Corporation

For many years, the Internal Revenue Service was hostile to the concept of professional incorporation. It took the position that despite the fact that a professional corporation was formed under its state's law and despite the fact that the professional corporation had conducted its affairs in conformity with state law, nevertheless, for tax purposes, this corporation would not necessarily be considered as a corporation, and, as a result, would not benefit from the significant tax advantages available to corporations. This hostility of the Service toward the professional corporation abated only after four court decisions adverse to the Service's position. Recognizing the Service's historical attitude, it is essential that every act of the professional corporation reflect its corporate status. All professional corporations (but particularly one-man professional corporations) must observe state professional corporation statutes strictly. Their "corporateness" must be unimpeachable. In their every day business transactions, professionals operating in corporate form must be constantly mindful that it is the *corporation* that is in the business of rendering professional services, and that the individual professional practitioner is an individual employed by the professional corporation to assist it in carrying out its business. Within that framework, the following incidents of practicing a profession in corporate form must be considered:

A. *Assets, Liabilities and Contractual Relations*

Since the corporation, and not the individual, is now conducting business, it follows that the corporation, and not the individual, must be possessed with the tools of the trade. It is necessary, therefore, that all of the assets used by the individual practitioner in the pursuit of his profession be transfered to the corporation when the practitioner incorporates his practice. The most common forms of assets transferred are bank accounts (which can be switched over into the corporate name); professional equipment; office furniture and fixtures; library; automobiles; and all other assets used in the conduct of the profession.

In similar fashion, it may be desirable that any liabilities incurred by the individual practitioner in the conduct of his profession be assumed by the corporation when the professional corporation is formed. The most common type of liabilities would include bank loans, chattel mortgages on equipment, and accounts payable. Usually, some consent on the part of the holder of these liabilities will be required in order for them to be assumed in the corporate name. Frequently, the individual practitioner will be required to guarantee the obligations personally. Nevertheless, if these liabilities can be assumed without adverse tax consequences, this assumption should be made by the corporation.

Along the same lines, any contracts entered into by the individual practitioner in the conduct of his profession, should, if possible, be transferred to the corporation. The most common types of contracts which would fall into this category are office leases and insurance policies. Here an important exception is worth noting. While insurance policies covering Workmen's Compensation, fire, theft and liability for accidents on the business premises, should be transferred to the corporation as insured, malpractice and similar insurance should be maintained both in the corporate name and in the name of the individual practitioner. The necessity to maintain this type of insurance in the individual name arises from a provision of Connecticut law which imposes upon the individual practitioner personal liability for his professional dereliction even if his practice is incorporated. As in the case of the transfer of liabilities, the transfer of individual contracts to the corporation frequently requires the consent of the other party to the contract and a personal guarantee of the obligation by the individual practitioner.

B. *The Professional Employee*

1. General Considerations

An individual engaged in the private practice of his profession in corporate form is in many respects in the same position as any other corporate employee. Put in a professional context, his employment is governed by the same characteristics as, for example, an engineer employed by a large aerospace corporation, or an accountant employed by a major bank. Thus, the professional employee of the professional corporation fills out a W-4 Withholding Tax form; is paid a salary by the professional corporation; has withholding tax, social security and other payroll deductions withheld from his periodic gross compensation; receives a W-2 form from the professional corporation at the end of the year indicating the gross compensation paid and the amounts of payroll deductions withheld; and operates under the direction and control of the corporation (even if the individual professional is the sole stockholder, director and officer of the corporation). As a corollary to this method of operation, the professional corporation files a corporate income tax return. The individual professional files an individual income tax return on Form 1040, but in contrast to the unincorporated professional, he does not file either a partnership income tax return or Schedule C of Form 1040 (Income from Trade or Business) which are filed only by individuals or partnerships conducting business in non-corporate form.

2. The Employment Contract

As further evidence of the arms length relationship between the professional corporation and owner-employee, it is standard practice to have in effect an employment contract between the professional corporation, as employer, and the individual professional, as employee. Such a contract normally provides for: (a) the duties to be performed by the professional employee for the professional corporation; (b) an undertaking that these duties are to be performed conscientiously and to the best of the individual professional's ability; and (c) the regular periodic compensation of the employee by the corporation and, usually, the terms under which he will be eligible to receive a bonus above and beyond his regular compensation.

It must always be borne in mind that such an agreement is standard practice even where the individual professional is the sole shareholder, director and officer of the professional corporation. Other provisions commonly found in employment agreements include: (a) the fringe benefits which are available to the corporate employee (which may include the use of an automobile, a pension plan, a profit sharing plan, group insurance and any other benefits that may be appropriate to the particular situation); (b) provisions for stock redemptions or "buy-outs" of stock held by employee shareholders (these are particularly valuable where a group practice is being conducted on a corporate basis); and (c) related provisions governing the death, disability, retirement or professional disqualification of the individual professional employee.

C. *Corporate Housekeeping*

In order to insure that the considerable tax benefits of professional incorporation will survive Internal Revenue Service scrutiny, the professional corporation must be in strict compliance with the state statutes authorizing professional corporations to exist. This requires the observance of certain corporate formalities which are characteristic of business corporations in general and professional corporations in particular. Among these are the following:

1. Preparing and Filing the Corporate Charter

Among the provisions commonly included in a corporate charter are the name of the corporation; the purpose for which the corporation is formed (e.g. "to practice medicine for pecuniary profit"); the location of the office of the corporation; the capital structure of the corporation and in some cases, other basic "ground rules" of corporate existence.

2. Preparing the Corporate By-Laws

Corporate by-laws generally deal with (a) the operational aspects of the corporation and (b) in many cases, the relationship between the respective stockholders of the corporation. Under the former category, various provisions govern the procedure for election and tenure of directors and officers of the corporation, and their powers and duties. Other provisions may set forth the frequency and times of meetings of the stockholders and Board of Directors, respectively, and provide quorum requirements. In providing for the relationship between the stockholders of the corporation, the by-laws function, in effect, as a contract binding all present and future stockholders of the corporation. Thus the by-laws may provide for the conditions under which stock in the corporation may be bought and sold by its shareholders; and may provide for the repurchase by the corporation or its shareholders of the stock of a fellow shareholder who retires, resigns, dies, or is professionally disqualified. Naturally, this represents only a partial list of what may commonly be found in professional corporate by-laws. By-laws must be drawn to meet the specific requirements of the professional corporation they govern.

3. Meetings

Even if a professional corporation is owned by a single stockholder and that stockholder serves as its sole director and officer, the existence of a corporation implies periodic "meetings" of the stockholders and of the directors. In this regard, it is advisable that directors' meetings be held not less than quarterly and stockholders' meetings not less than annually. In addition to regularly scheduled meetings, it is sometimes appropriate to hold "special" meetings of the directors or the stockholders. Special meetings will customarily be held to consider proposed corporate action of more than routine significance to be corporation. Such action might be the sale of a significant part of the corporate stock or assets, the purchase of a major piece of equipment, the mortgaging of significant corporate property, or the entering into of a significant corporate contract.

4. Reports

As with all other Connecticut corporations, a professional corporation must file an annual report with the Secretary of State.

D. *Holding Out the Corporation to the Public*

The everyday operating procedures of a corporation must consistently reflect that it is in fact a corporation and not an individual or group of individuals. Among the everyday details which convey this message are the following:

1. Corporate Name

Connecticut law requires that the corporate name of each professional corporation must include at the end of the name the words, "Professional Corporation" or the abbreviation "P.C."; and must contain "either a word or words descriptive of the professional service to be rendered by the corporation . . . or the last name of one or more of the present, prospective or former shareholders or of persons who were associated with a predecessor or person, partnership, corporation or other association or whose name or names appeared in the name of such predecessor organization." Thus, if John Doe, M.D., decides to incorporate his practice, the corporate name he selects might be *John Doe, M.D., P.C.* This name should appear on any professional shingle or on any door-sign, on letterheads, billheads, professional cards, prescription pads, telephone listings and, in general, any documents circulated between the corporation and its patients.

2. Financial Separation

The corporation must be kept financially separate from its individual professional employees. Thus, all billing is done in the corporate name. When fees are paid, they are deposited in the corporate bank account. Should a patient issue a check payable to an individual professional employee, that check should be endorsed over to the corporation and deposited in the corporate bank account.

3. Everyday Business Transactions

All contracts and other business dealings should be conducted in the corporate name. As mentioned above, these might include office leases, insurance policies, etc.

If all of the aforementioned practices are followed diligently, the professional corporation has a reasonably good opportunity to sustain its corporate status in the event of any Internal Revenue Service inquiry.

In this presentation, the author has attempted to summarize, for the non-lawyer, some of the factors to be considered in deciding whether or not to incorporate your practice. Naturally, this article is not the law. The law is embodied in the highly complex provisions of the Internal Revenue Code, in the Regulations adopted under the Code, and in the numerous interpretive rulings issued, from time to time, by the Internal Revenue Service. All of these must be considered, in depth, with the guidance of your attorney and your accountant.

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CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1972 Annual Meeting of the House of Delegates is scheduled to be held in the Terrace Room of the Hartford Hilton Hotel, Hartford, on Tuesday, April 25. Commencing at 8:30 A.M. Following luncheon, the House will reconvene for the completion of its business.

Frederick C. Weber, Jr. President
Kenneth F. Brandon, Speaker of the House
Louis C. Backhus, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

Summary of Actions
Council Meeting
Wednesday, January 19, 1972

I. Attendance

Present in addition to the Chairman, Dr. K. F. Brandon, and the Vice-Chairman, Dr. D. A. Grendon, were Drs. Weber, Jr., Cramer, Spitz, Backhus, Nolan, Granoff, Dean, Gardner, Fabro, Hess, Bradley, Rem, Johnson, Ragland, Jr., Harwood, Pelz, Palomba, Roch, Nemoitin, VanSyckle, Friedberg, Luby, Harkins, LaBella, Root, Jr., Freedman, Dambeck and Klare.

Also present were: Mrs. Lindquist, Mr. Sullivan, Mr. Tomat, Mr. Gordon (HCMA), Mr. Olson (FCMA), Dr. West (NHCMA), Dr. Goldstein (HCMA) and Dr. Richards.

Absent was: Dr. Wilson.

In Memoriam

The Chairman formally apprised the members of the Council of the sudden death of Harold D. vonGlahn, Old Lyme, Associate Councilor from the New London County Association, on January 8, 1972. Recalling the high esteem in which Dr. vonGlahn was held as a colleague and as a friend, the members and guests of the Council joined in a moment of silent prayer in his memory.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meetings of December 9, 1971 and December 12, 1971.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Stanley J. Alexander, 760 Saybrook Road, Middletown (M)
Philip G. Baker, 26 Elm Street, Winsted (L)
Theodore M. Ebers, P.O. Box 821, Sedona, Arizona (H)
John N. Gallivan, 951 Ridge Road, Wethersfield (H)

Date of Next Meeting

The next meeting of the Council was scheduled for Thursday, February 17, 1972.

III. Old, New and Special Business

Election of Student Members

It was VOTED to elect to Student Membership five Connecticut residents who are enrolled as students in American medical schools. A list of those elected will be published in an early issue of the Journal.

Report—Ad Hoc Committee on Utilization of "Combined (Obstetrical) Units"

It was VOTED to accept for filing, and with commendation, a report filed for this Ad Hoc Committee by its chairman, Stuart Ragland, Jr., Colebrook. In brief, the report informed the Council that the Ad Hoc Committee had met with the State Council on Hospitals (10/7/71) as directed; had advanced and promoted the position of the House of Delegates which advocates liberalization of the combined unit program; had heard the arguments of the representatives of the Connecticut Society of American Board Obstetricians and Gynecologists which favored maintenance of the status quo for such program; and had been assured that, in due course of time, the Council on Hospitals would make subject recommendations to the Public Health Council and the Commissioner of Health. It was Dr. Ragland's opinion that the recommendations would probably advocate some degree of liberalization of the program.

Report—Committee on PRO's, Foundations and HMO's

It was VOTED to accept for filing a progress report filed for this Committee by its chairman, Sidney L. Cramer, Hartford. In brief, the report informed the Council that the Committee had been making a continuing study of the three related subjects; that the Committee had determined to give first priority to the development of a Peer Review Organization for Connecticut; and that the Committee recommended to the Council that a PRO be appointed and authorized to serve formally, on a "pilot study" basis, as a statewide peer review organization for the Medicare B Program.

It was further VOTED to approve the latter recommendations as follows:

(1) That the Council direct the President, in consultation with the Chairman of the Council and the Chairman of the Committee on PRO's, Foundations and HMO's, to appoint a committee of 10-12 qualified members of the Society, to be designated the "CSMS Peer Review Organization for the Medicare B Program", and name the chairman thereof.

(2) That said PRO be authorized, on a one-year pilot basis, to serve as an official CSMS-sponsored peer review organization for the Medicare B Program, in cooperation with the Connecticut General Insurance Company.

(3) That the PRO be authorized to utilize the modalities and resources outlined in the report (consultants, computerized data, CSMS Relative Value Guide, county medical associations, etc.) to assist the PRO in discharging its review functions with the Medicare B Program.

(4) That the question of compensation for members serving on the PRO be explored with Connecticut General by the members of the PRO appointed by the President et al, and that a subject report with recommendations be made to the Council when such exploration has been completed.

Presentations—CSMS Financial Aid Program for Medical Students

Pursuant to the financial aid program for medical students approved by the House of Delegates on November 17, 1971, President Weber presented CSMS checks in the amount of $3,000 each to representatives of the Yale and UConn Medical Schools. Accepting the checks were: For YUSM—Dr. Howard Levitin, Associate Dean for Student Affairs, for UCMS—Dr. William Fleeson, Professor of Psychiatry and Associate Dean for Student Affairs. Also present as a guest of the Council was: Mr. Louis Kaplan, Assistant to the Dean of YUSM. This financial aid fund, as outlined by Dr. Weber in making the presentations, "is being initiated by the Society, on behalf of its members, in recognition of the need of many medical students to have resources available to them when, from time to time, their major resources may prove insufficient to meet their total financial obligations".

An experience report will be filed with the House of Delegates at its 1972 semi-annual meeting, and, based on the experience, decisions will be made concerning its future continuance.

Progress Report—Judicial Committee

J. Alfred Fabro, Torrington, chairman of the Judicial Committee, reported further on a situation obtaining at a Connecticut hospital in which a physician is being denied promotion to attending staff status and concerning which the Council had endorsed the position taken by the Judicial Committee that the physician was entitled to receive in writing the reasons for such denial of promotion.

Dr. Fabro reported that while he had received several assurances over the past 6 months that the physician in question would be given said reasons in writing by the medical board and/or the board of trustees, such reasons in writing had not yet been forthcoming.

Following a lengthy discussion of this matter, the Council VOTED to authorize the chairman of the Judicial Committee to write a letter to the incumbent (new) president of the medical board of the hospital concerned, reaffirming the Council's position in this matter; advising him of the Council's continuing dissatisfaction that the situation has not yet been resolved, despite previous assurances that it would be; and urging that he take appropriate steps to inform in writing the physician concerned of the reasons why his application for attending staff status had been and is being denied. In composing the aforesaid communication, Dr. Fabro is to consult with Kurt Pelz, Clinton, a member of the Judicial Committee.

Connecticut Medical Service, Inc.

The entire situation relating to the policy of CMS to terminate Participating Physician agreements, effective 1/1/72, for all PP's who had not signed to participate in the Century Contract was carefully reviewed. Recognition was made of: (a) the fact that the National Association of Blue Shield Plans had not yet responded to the question as to whether the CMS policy was in accordance with NABSP's concept of voluntarism; (b) the decision of the judge who heard the Society's request that a temporary injunction be issued to prevent CMS from implementing its policy on 1/1/72 (the judge's decision—Request denied); and various communications received from individual members and groups of members expressing opinions, both pro and con, as to the CMS policy itself and as to the Council's decision to take legal action concerning same.

N.B.: As information, the following excerpt from the agenda of this meeting is made a part of these minutes:

Decision of the Court: In a 10 page memorandum, Judge Rubinow lists his findings with respect to the various arguments presented by both sides during the course of the hearing and states his conclusion as follows: "The plaintiffs have shown no legal right on which the court may deny the defendant (CMS) the power to terminate the participation contracts (with physicians) in accordance with its memorandum of October 26, 1971. This makes it unnecessary to decide whether (the Connecticut) State Medical (Society) and the (Hartford) County Medical (Association) have 'standing' to prosecute the present action".

Having discussed all known channels through which CMS's alleged violation of antitrust laws might be pursued through legal activities, the Council VOTED (16-8) to take no further legal action in this matter at this time. The attorney who represented the Society at the December court hearing is to be apprised of this decision.

It was further VOTED to direct the President and the Chairman of the Council to urge each of the component County Medical Associations to seek to determine the consensus of opinion among the Association's membership concerning the desirability of taking further legal action in the matter; also ,the consensus of opinion concerning the continuance of the present CSMS policy re advancement of the concept of "usual and customary" (prevailing and reasonable) charges or changing the policy to advance the concept of "fee schedules" as the basis for third party payment for physicians' services. The objective of seeking the consensus of membership opinion on these matters is to enable the Council, from the knowledge gained by the County Associations' representatives on the Council, to act in concert with the known wishes of the majority of members.

The CSMS staff is to furnish each County Association secretary with a copy of the material considered by the Council at this meeting, and a copy of a memorandum obtained from legal counsel outlining the options, alternatives and prospects relating to the possibility of undertaking further legal action against CMS with respect to its present "all-or-none" policy on physician participation in its contracts.

Report—Committee on Hospitals

It was VOTED to accept for filing a revised report submitted by the Committee concerning a mechanism through which to establish continuing liaison between the Council and hospital medical staffs, and it was further VOTED to approve the new mechanism proposed and its implementation. In brief, the report recommends establishing liaison "initially at meetings of hospital chiefs of staff at the county level (initiated by County Medical Associations, if possible) and that where this is not feasible or practical, the Committee on Hospitals will provide the necessary mechanism for such meetings."

Nomination for AMA Advisory Committee on Cancer

It was VOTED to nominate E. Tremain Bradley, Norwalk, for possible appointment to this new Advisory Committee which the AMA is presently forming. While the details are not presently known, it is assumed that the Committee is being formed to play some part in the "War on Cancer" legislation recently enacted by the Congress.

Nomination for Connecticut Medical Examining Board

Received as information was notice given by President Weber that, after due and extensive consideration, he had selected Charles W. Chace, Middletown, a generalist, to nominate to the Governor for the latter's appointment to the Connecticut Medical Examining Board as a replacement for Harold D. vonGlahn, Old Lyme, deceased 1/8/72. If appointed, Dr. Chase will serve the balance of the five-year term, 1/1/69-12/31/73.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on January 19, 1972. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by an interested member of the Society.*

SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, February 17, 1972

I. Attendance

Present in addition to the Chairman, Dr. K. F. Brandon, and the Vice-Chairman, Dr. David A. Grendon, were: Drs. Weber, Spitz, Backhus, Nolan, Granoff, Dean, Gardner, Fabro, Hess, Rem, Harwood, Pelz, Wilson, Nemoitin, Van Syckle, Friedberg, Harkins, LaBella, Root, Jr., Freedman, Sprecace and Klare.

Also present were: Mrs. Lindquist, Mr. Olson (FCMA), Mr. Tomat, Mr. Sullivan and Dr. Richards.

Absent were: Drs. Cramer, Bradley, Johnson, Ragland, Jr., Palomba, Roch, Luby and Dambeck.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of January 19, 1972, with the exception that, under "Referral of Question of Medical Ethics" (Page 6), the words "is presumed to have been initiated or approved for publication (by the CMS Executive Vice-President)" be changed to "was initialed for publication."

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Edward V. Carvey, 121 Broad Street, Wethersfield (H)—1/1/72

Helen K. Ferguson, 172 Niantic River Road, Waterford (NL)—1/1/72

Louis H. Gold, 21 Woodland Street, Hartford (H)—1/1/72

Morris Y. Krosnick, 119 West Park Avenue, New Haven (NH)—1/1/72

John C. Larkin, New Britain General Hospital, New Britain (H)—1/1/72

Samuel D. Lewis, 2760 South County Road, Palm Beach, Florida (H)—1/1/72

Jacob H. Lubchansky, 27 Broad Street, New London (NL)—1/1/72

Nicholas A. Marinaro, Cedarcrest Hospital, Newington (H)—1/1/72

Charles A. Murphy, 300 Bayberrie Drive, Stamford (F)—1/1/72

Albert U. Peacock, 85 Jefferson Street, Hartford (H)—1/1/72

George J. Rosenbaum, 647 New Britain Avenue, Hartford (H)—1/1/72

Francis J. Ryan, 65 Cliffmore Road, West Hartford (H)—1/1/72

William Beecher Scoville, 85 Jefferson Street, Hartford (H)—1/1/72

Date of Next Meeting

The date of the next meeting of the Council was set for Wednesday, March 22, 1972.

III. Old, New and Special Business

Communication—Department of HEW re Medicaid

It was VOTED to receive for filing a letter received from the Department of HEW in response to a resolution adopted by the CSMS House of Delegates on 11/17/71 on the subject of "Inequities Under the Medicaid Law Affecting Medicaid Beneficiaries and Practicing Physicians." Copies of the resolution were also sent to the State Commissioners of Welfare and of Finance and Control but were not responded to or even acknowledged by the Commissioners. Recognizing that some of the statements made in the HEW communication warrant discussion with State Commissioners, the Council VOTED to send a copy of the HEW letter to the Commissioner of Finance and Control, the Commissioner of Welfare and to the members of the CSMS Liaison Committee with the Welfare Department, and to direct the Liaison Committee to seek to arrange a meeting with said Commissioners to engage in such discussion and to report to the Council concerning same.

Report—Committee on Cooperation with Medical Schools re "MECO"

It was VOTED to receive for filing a report of the Committee on the "MECO" project of the Student American Medical Association and to authorize the Committee, with staff assistance, to implement the Committee's recommendations as follows:

(a) To publicize "MECO" and its objectives to the Society's membership, noting that the program is endorsed by the Society.

(b) To have the CSMS office constitute a source of information about the program, and assign a staff person the duty of furnishing such information to inquirers.

(c) To assist SAMA representatives in Connecticut, in cooperation with representatives of the Connecticut Hospital Association, in the matching process between medical student and community.

Report—Cleveland Symposium on Socio-Economics of Medical Care

It was VOTED to receive for filing, and with commendation, a report filed by Sidney L. Cramer, Hartford, on the proceedings of the "Second Annual Invitational Symposium on the Socio-Economic Aspects of Medical Care", Cleveland, 11/16/71. It was further VOTED to distribute information copies of the report to members of the Committee on Hospitals, the Committee on Third Party Payments, the Committee on PRO's, Foundations and HMO's and other committees that staff may deem appropriate.

Report—Committee on Preliminary Study of Nominations

It was VOTED to approve, with several amendments, a slate of officers, committees, etc. for 1972-73 (or other specified term) prepared by the CPSN and to transmit the slate approved to the House of Delegates at the annual meeting on April 25 with Council recommendation for election by the House.

In conjunction with approving the slate of nominees, it was further VOTED to abolish several Council-elected committees as follows: The Committee on Medicine and Religion; the Liaison Committee with Connecticut General on Medicare B; the Committee on Health Care of the Poor.

Request for Nominees—State Advisory Drug Council

Being advised by Health Commissioner Foote that Benjamin Wiesel, Hartford, a CSMS nominee serving on the State Drug Advisory Council was resigning his post, and requested by the Commissioner to nominate "about three physicians" from which the Governor could appoint one to replace

Pre-Sate®
(chlorphentermine HCl)

CAUTION: Federal law prohibits dispensing without prescription.
Indications: Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (*i.e.*, several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.
Contraindications: Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.
Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.
Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.
Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.
Usage In Children: Not recommended for use in children under 12 years of age.
Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.
Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.
Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.
Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.
Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.
How Supplied: Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.
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Dr. Wiesel, the Council VOTED to submit three such nominees as follows:

Mario Leicach, Hartford
Clayton B. Weed, Stamford
Alan R. Gurwitt, New Haven

Communication—Associate Dean, UConn School of Medicine

It was VOTED to receive for filing, and with appreciation, a letter from Associate Dean William Fleeson of the UConn School of Medicine in which the thanks of the Medical School and the University are expressed to the Committee on Cooperation with the Medical Schools of Connecticut, to the Council and to the House of Delegates for developing and implementing the CSMS Financial Aid Program for Medical Students, approved by CSMS last November and put into operation in January of this year. Since the letter was addressed to President Weber, it was further VOTED to request the President to acknowledge it for the Council.

Report—Committee on State Legislation

Having heard a verbal report on a number of subjects having to do with legislation and legislative activities presented by the Committee chairman, Isadore H. Friedberg, Hartford, the Council VOTED to take several actions as follows:

(a) *Health Care Commission Bill*: It was VOTED to oppose the bill establishing a Health Care Commission Bill being proposed by Representative Cohen and to authorize the Committee on State Legislation to support any substitute bill which, in its judgment, is in the best interest of the people of Connecticut.

(b) *Physicians at the Capitol*: It was VOTED to authorize the Committee to try to arrange for a physician to be available to the Society's legislative agent at all sessions for the purpose of advising on legislative matters and informing legislators concerning CSMS positions on specific bills.

(c) *Communication to Health Commissioner re Optometrists*: Being apprised by the Committee that the Section on Ophthalmology is requesting Commissioner Foote to investigate the modus operandi of an "eye care clinic" reported to have been set up in Bridgeport by a group of optometrists, the Council VOTED to urge Dr. Foote to look into the situation, as requested by the Section. The issue in contention, according to the Section, is that publicity given the clinic suggests that examinations are being

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INDICATIONS: Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses, such as the common cold, seasonal allergies, sinusitis, rhinitis, conjunctivitis and otitis. In these cases it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions, thereby affording relief from nasal stuffiness and postnasal drip.
CONTRAINDICATIONS: Hypersensitivity to antihistamines of the same chemical class. Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age. Because of its drying and thickening effect on the lower respiratory secretions, Dimetapp is not recommended in the treatment of bronchial asthma. Also, Dimetapp Extentabs are contraindicated in concurrent MAO inhibitor therapy.
WARNINGS: *Use in children:* In infants and children particularly, antihistamines in overdosage may produce convulsions and death.
PRECAUTIONS: Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery, etc. Patients receiving antihistamines should be warned against possible additive effects with CNS depressants such as alcohol, hypnotics, sedatives, tranquilizers, etc.
ADVERSE REACTIONS: Adverse reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash, urticaria, leukopenia, agranulocytosis and thrombocytopenia; drowsiness, lassitude, giddiness, dryness of the mucous membranes, tightness of the chest, thickening of bronchial secretions, urinary frequency and dysuria, palpitation, hypotension/hypertension, headache, faintness, dizziness, tinnitus, incoordination, visual disturbances, mydriasis, CNS-depressant and (less often) stimulant effect, anorexia, nausea, vomiting, diarrhea, constipation, and epigastric distress.
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made for "eye diseases" and that medication ("drops") is being used in conjunction with refractions.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on February 17, 1972. Detailed minutes of the meeting are on file at 160 St. Ronan St., New Haven, for perusal by any interested member of the Society.*

NEW BOOKS IN REVIEW

IDENTIFICATION OF ASTHMA. The Ciba Foundation's report of Study Group #38. edited by Ruth Porter and Joan Birch. Published in 1971 by Churchill Livingstone, Edenburgh and London.

Reviewed by: ARNOLD B. RILANCE

This very interesting monograph is authored by twenty-six outstanding authorities in the field of chronic lung disease, most of whom are British, with several representatives from Canada, the United States and Australia.

In the Chairman's opening remarks, he states: "Our aim is to define asthma". He continues: "Only recently have we began to ask which generation of bronchii or bronchioles are affected; is all lung muscle equally involved; do bronchiolar muscle contractions and mucosal inflammation always go hand in hand or can they be disassociated or even occur separately in different parts of the lung?". He points out that persistent ventilation perfusion defects which occur after the acute attack has subsided indicate that smaller airways take far longer to return to normal than had previously been assumed to be the case. In this monograph, all aspects of obstructive lung disease are touched upon, although many basic concepts are not given consideration. The main theme of the monograph is an attempt to differentiate between chronic asthma and chronic bronchitis, which may simulate each other. The immunological basis for asthma is given a reasonably thorough discussion and newer concepts of the immunological basis for the asthmatic reaction are discussed.

In the final conclusion, the authors in the study group decided that asthma could not be defined on the information at present available. This does not mean that, in the classical form of asthma, one cannot with reasonable accuracy arrive at such a diagnosis. It does point out, however, that a sharp differentiation between the clinical and physiological disturbances in chronic obstructive bronchitis and bronchial asthma cannot be clearly defined.

This is a thought provoking monograph which touches on newer concepts and understanding of the disease, bronchial asthma.

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APRIL 25, 26, 27, 1972
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Placement Wanted

In the past month the Placement Service has received a great number of resumes from physicians interested in locating in Connecticut. Many will be completing in the summer their residency and/or their military obligations. Space does not permit us to list each candidate separately. Please refer to the following listing and contact the Placement Service for more information. (865-0587)

Allergy—Three Board certified or Board eligible candidates have resumes on file.

Anesthesiology—Six candidates have indicated interest in locating in Connecticut. Three with Connecticut licenses.

Dermatology—Three have submitted resumes. One Board eligible; one Board certified.

Family Practice—Twelve have submitted resumes for consideration.

Internal Medicine—Fifty-one resumes are on file. Many sub-specialties.

Neurosurgery—Five candidates have indicated interest in settling in Connecticut.

OB/GYN—Two resumes are on file. One Board certified; one Board eligible.

Opthalmology—Twelve resumes are on file. Most will be available in July.

Orthopedics—Nine have submitted resumes for placement in Connecticut.

Otolaryngology—Four resumes are on file. One with Connecticut license.

Pathology—Seven have indicated interest in locating in Connecticut.

Pediatrics—Six have resumes on file.

Psychiatry—Seven have indicated interest in locating in Connecticut.

Surgery—Thirty resumes are on file. Many sub-specialties.

Urology—Nine have indicated interest in Connecticut communities. Eight are Board Eligible; one Board certified.

Allied Personnel—EEG Technologist—31 years of age. Nine years of experience. Wishes position as instructor in clinical EEG Technology or technologist in charge of new laboratory. Available June 1. Presently at University of Kentucky completing degree program. Richard F. Wilmarth, 133 Brown Avenue, Lexington, Kentucky 40505.

Anesthesiology—41 years of age; Interested in large hospital; respiratory therapy and chest disease. Available early 1972. Board Certified.

Dermatologist—American Board Certified; Connecticut License; Interested in Group, Associate or Institutional Practice in large or medium sized Connecticut community. 31 years of age. Nira R. Silverman, M.D., 91 Corbin Road, Hamden, Connecticut 06517.

Family Practice—28 years of age. Interested in group practice. Available mid-1972. Arthur L. Stein, M.D., 1117 Grant Boulevard, Syracuse, New York 13203.

General Practice—Connecticut license. Prefers solo practice. 50 years of age. Available immediately.

General Practice—28 years of age. Solo, group or associate practice. Connecticut license. Large or medium sized community. One year of residency in surgery. Arthur E. Woolfson, M.D., 33 Highland Street, New Britain, Connecticut.

General Practice—41 years old. Desires rural area. Solo practice. National Boards. W. Dean Pope, M.D., Box 490, Rangeley, Maine 04970.

Industrial Medicine—40 years of age; Connecticut and National Boards. Available early 1972.

Industrial Medicine—48 years of age; Connecticut license; Presently with firm in New Jersey. Wishes to relocate. Available immediately.

Neuropsychiatry—48 years old; Connecticut License in process. Solo, group, associate, institutional. Interested in E.E.G. Experience in research and teaching. Andre J. Angyan, M.D., Ph.D., 321 Orchard Drive, Pittsburgh, Pennsylvania, 15238 (412-828-5509).

Ophthalmology—30 years of age; National Boards, Board eligible; solo or associate type practice. Available March 1972.

Pathology—46 years of age; Board certified; Prefers medium size community; Connecticut License; Available February 1972.

Radiologist—Holds Connecticut license. Temporary coverage effective April 21, 1972. Trained for the past four years in London. Danniel P. McCarthy, M.D., 1, Holyoake Walk, Ealing, London W5, England.

Radiology—42 years old; Board Certified; FLEX; Presently teaching. Available immediately.

Summer Employment Opportunities: Camp physicians; part time or vacation coverage. Medical students seeking hospital or laboratory positions. Contact: Connecticut State Medical Society—203-865-0587.

Placement Opportunities

Allergist—Wanted as soon as possible. Must be board eligible for a two-man allergy practice which now requires a third man. Work week is four days; every third weekend off. Early partnership for right man guaranteed. 100,00 population. Centrally located in a university town. Connecticut license required. First year-five figure salary. Area Code 203 346-1575.

Anesthesiologist—To join three man group in 180 bed community hospital. Interest in inhalation therapy and respiratory physiology important. Recent or near future residency graduate acceptable. Living conditions excellent in semi-rural area with nearby University of Conn. and State College affording many recreational and cultural advantages. Please contact Anesthesia Associates, P.O. Box 23, Willimantic, Connecticut 06226. Tel. 423-9201.

Anesthesiologist—To join Board certified chief of anesthesiology in small community hospital. No OB. Salary negotiable. If interested contact administrator or chief of anesthesiology. Johnson Memorial Hospital, Stafford Springs, Connecticut 06076.

Connecticut Based Insurance Company: Three physicians needed: Employee Health Clinic; Claims Review; Medical Evaluation for Underwriting Purposes. Connecticut license. Good benefits.

Director of College Health Service—Full time position; September, 1972; C. B. Crampton, M.D., Wesleyan University, Middletown, Connecticut 06457.

Emergency Room Physician—To complete four-man group. 100-bed, full service hospital. Solid backup in all specialties and most subspecialties from Active Staff. Central Connecticut community midway between Hartford and New Haven. Must be eligible for Connecticut licensure. Attractive salary, excellent benets. Resumé to Chief of Staff, World War II Memorial Hospital, Meriden, Connecticut 06450.

Family Practice—Southwestern Litchfield County. Community hospital. Conveniently located. Community physicians also searching for pediatrician and Ob/Gyn to enter private practice.

Family Practice—Growing community seeks family physicians. North-central Connecticut. Approximately 47,000 population. Several hospitals in the area. New hospital in planning stages. Number of specialists in town. Conveniently located.

Associate in General Practice: Busy general practice in Milford, Connecticut including pediatrics, Obstetrics and Gynecology, and some surgery (major and minor). New fully equipped office across the street from 200 bed open staff hospital. Boating, fishing and beaches 5 minutes from office. Yale-New Haven Medical Center and Yale cultural facilities 15 minutes away. Salary for one year with partnership to follow if agreeable. Please contact: Barry M. Winters, M.D., 73 Golden Hill Street, Milford, Connecticut 06460.

General Medicine and Internal Medicine—Northwestern Connecticut community seeking to attract practitioners. Associate type practice possible.

Internist—A third Internist is needed to join two other Internists in the town of Manchester, Connecticut. Office located across the street from a 300 bed community hospital which is currently in the second of a three stage building program. Manchester is located fifteen minutes from Hartford, one hour from New Haven, one hour and a half from Boston and two hours from New York City. For further information contact: Harold J. Lehmus, M.D., or David L. Warren, M.D., 56 Haynes Street, Manchester, Connecticut 06040. Telephone: 203-646-1167.

Internist—Preferably Board Certified or eligible, for chronic disease and cancer hospital having sections for TB in adults and children. 35 hr. week, 11 paid holidays, sick leave, 3 weeks vacation after one year of service. Salary level: $23,227-28,333. Paid health insurance and minimum charge for life insurance. Apartment available for physician with small family. Write Medical Director, Uncas-on-Thames Hospital, Norwich, Connecticut 06360.

Ob/Gyn—Community in western Connecticut in search of physician to open private practice. Community's growth requires additional medical services.

Occupational or Industrial Medicine—Two Connecticut post offices need staff physicians. Connecticut license. Part or full time.

Orthopedic Surgeon—Central Connecticut area. Community Hospital. Group practice with three other orthopedic surgeons.

Pediatrician—Community physicians feel that another pediatrician is needed. Central section of the state. 40% of population 18 years of age and under.

Pediatrician—currently board-eligible or board certified. Full-time position. Salary negotiable. To practice family oriented medicine in a private, non-profit neighborhood health center. For further information please contact Evans H. Daniels, Jr., M.D., Medical Director, Community Health Services, Inc., 1023 Albany Avenue, Hartford, Connecticut, 06112. Telephone 549-1423.

Proctology—Lucrative practice available in New Haven. Physician deceased. Fully equipped office. Contact: A. M. Murray 203-787-4161.

Senior Physician—positions available at Norwich Hospital. Primary responsibility for medical care of geriatric and mentally ill patients in a community oriented, geographically unitized hospital with many forward looking, exciting programs. Starting salary $20,465, many fringe benefits, hosuing available. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

Urology—Interested in an associate. Large, Southwestern Connecticut shore community.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT

Meeting Notices

The information on this "notices" page is offered as a service of all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the month preceding, date of issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

GENERAL

April 25-27, 1972—Tuesday-Thursday
180th Annual Meeting of the Connecticut State Medical Society
Theme: Clinical Pharmacology
Hartford Hilton, Hartford

September, 1971-May, 1972
Lecture Series—Each Tuesday
Basic Sciences As Related to Clinical Medicine:
Infectious Diseases, Coronary Care Problems, Diagnosis and Treatment of Tumors
Lawrence and Memorial Hospitals
New London, Connecticut
Contact: Edward Gipstein, M.D.

April 17-21—Monday-Friday
The American College of Physicians
53rd Annual Session
Atlantic City, New Jersey

April 14-16—Friday-Sunday
The American Society of Internal Medicine
Sixteenth Annual Meeting
Atlantic City, New Jersey

INTERNAL MEDICINE

April 5-7—Wednesday-Friday
Cardiology for the Internist
Baylor College of Medicine
Houston, Texas

1972 COUNTY ANNUAL MEETINGS

March 16—Thursday—Windham

March 23—Thursday—New Haven

March 28—Tuesday—Tolland

April 4—Tuesday—Fairfield

April 6—Thursday—New London

April 11—Tuesday—Litchfield

April 13—Thursday—Middlesex

April 19—Wednesday—Hartford

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Abortion Complications In New York

(*Lancet* II, 773, October 2, 1971) The law liberalizing abortion in New York State came into force July 1, 1970. In a series of preliminary reports on the first few months of the new law on abortion Pakter, Harris and Nelson list the complication rates in relation to method of abortion, week of gestation and type of hospital.

Suction, dilatation and curettage, and saline instillation are the three most common methods used to terminate pregnancies in 43,329 abortions analyzed. They consider infection, retained tissue, perforated uterus, hemorrhage, and failed abortion.

with D & C a total of 8.9 complications occurred

with suction 7.7 complications

with saline 35.0 complications

all methods 12.6 complications were encountered.

Knowledge of the patients Rh status and provision of Rh gamma globulin in at-risk cases is now thought to be ideal abortion practice but in many cases this was not done.—L.H.N.

Reference, Legal Abortions in New York State (Modern Treatment 1971, 8: No. 1) Edited by George Schaeffer, M.D. New York. *Harper and Row* 1971, pp. 222.

Clinical Experience With Permanent Demand Pacemakers

(*Mayo Clinic Proceedings*, 46: 44, 1971, McNonahay, D. R. et al.) In an initial 2 year experience with a permanent demand pacemaker, 64 patients received 80 units, 66 by transvenous endocardial electrode placement and 14 by transthoracic epicardial placement. The symptoms arose from third degree A.V. block in 39 patients, partial A.V. block in 18 and sinus node disease in 7.

Early complications related to pacemaker implantation occurred in 23 patients (2 deaths) and late complications (excluding late battery depletion occurred an average of 20.2 months after implantation.

Among 41 patients who have had units for more than one year, 34 have achieved an excellent clinical result during 12-31 months of pacing and 5 (12%) have died.—L.H.N.

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Plan New Horizons

Our country is spending billions of dollars each year to win friends around the world. Our auxiliaries with the help of our International Health Activities can accomplish great results in this field for the project appeals to many women who are not motivated by our other service projects. I.H.A. helps bring the joy of good health to millions of suffering people.

No matter how small the community, and we do have some small communities in Connecticut, there are international contacts that can be found for meeting programs. Perhaps you can find a Peace Corps worker recently returned from an unusual assignment who would like to talk to your members. Ask each doctor's wife who has traveled during the past year or who is going to visit some foreign country to briefly describe some health aspect of the country she toured.

Many members of our auxiliary and community do not know about the medical collection agencies and how they manage, with volunteer help and donations, to provide health care in far outposts. Those outside the auxiliary may be invited to a "Show and Tell" program illustrating the many things that can be made to send to the agencies. Our auxiliary has done a good job of knitting leper bandages and collecting medical journals in the past years. Perhaps we can revive those programs again! No matter what size your auxiliary, working for a collection agency is a worthwhile and satisfying project. (A list of agencies may be obtained from national headquarters or our state chairman.)

Doctors' wives in Delaware collected seventy-five pairs of used shoes and $1500. worth of new shoes to be used as corrective footwear for patients treated by doctors on the S.S. Hope while it was docked in Jamiaca. Six large cartons of orthopedic braces were sent from a leading children's hospital in that state.

Doctor's wife-to-doctor's wife is another good program for any sized auxiliary, but can be an especially rewarding experience for the small auxiliary. Every member might be persuaded to accept a doctor's wife "pen pal" in a foreign land. Reports, with pictures and letters, would make an interesting membership meeting. And one which wouldn't be costly!

Hospitality to foreigners may be something you are doing without even thinking of it as I.H.A. If you have a situation where it is possible, such as a medical school with foreign students, invite their wives to a meeting, introduce them and ask each one to tell something about the health needs in her country. In return, answer their questions about America, and help to solve their problems. New Haven and Middlesex counties have had very successful International Dinners recently. What an enjoyable way to extend goodwill across the seas.

Be a force in your community toward good relations with visitors from far lands. Exchange experiences and ideas with foreign residents. Give a foreign student a home away from home. Is there a need for translation teams to aid foreign speaking hospital patients in your area? Whatever the need, be helpful in providing the answers and make more friends for our country and for medicine. You'd be surprised at the "mistaken" ideas a young boys visiting hockey team from Sweden had about our manner and way of life here in Connecticut!

Think I.H.A. when your county plans its calendar. We've been doing a little, now let's do a lot!

Electrocardiogram of the Month:

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Normal Variants Mistaken as Evidence of Heart Disease II-ECG Mimic of Acute Anterior Wall Injury or Pericarditis

Upward displacement of the ST segment in the chest leads may occur in a significant number of normal subjects and especially in members of the black race. Such ST displacements are attributed to earlier repolarization in the area of the ventricle underneath the electrode.

Two different forms of this type of ST displacement are recognized. The more common one is characterized by the finding of concave ST elevation ending in a tall T wave usually most pronounced in leads V3 through V6. The R wave is quite tall in the leads exhibiting the ST displacement (Fig. 1). At times there may also be found terminal inversion of the T wave in these leads. The less common form of the ST variant consists of an ST elevation usually of the saddle-back shape and most pronounced in leads V1 and V2 (Fig. 2). The T waves in these leads may or may not be inverted.

Elevation of the ST segment in the chest leads is also found in hearts with recent damage to the anterior septal area either as a result of coronary artery disease or contusion. Acute pericarditis may also produce concave ST elevations initially limited to the chest leads. To compound the possible confusion even further serial studies in normal subjects exhibiting the physiological variant may show variable ST displacement due to alterations in sympathetic tone.

When ECG patterns as described above are found on routine workup of patients or even in patients complaining of chest pain they should be considered to represent a normal variant until proven otherwise by physical examination, serial ECG study, and other laboratory tests.

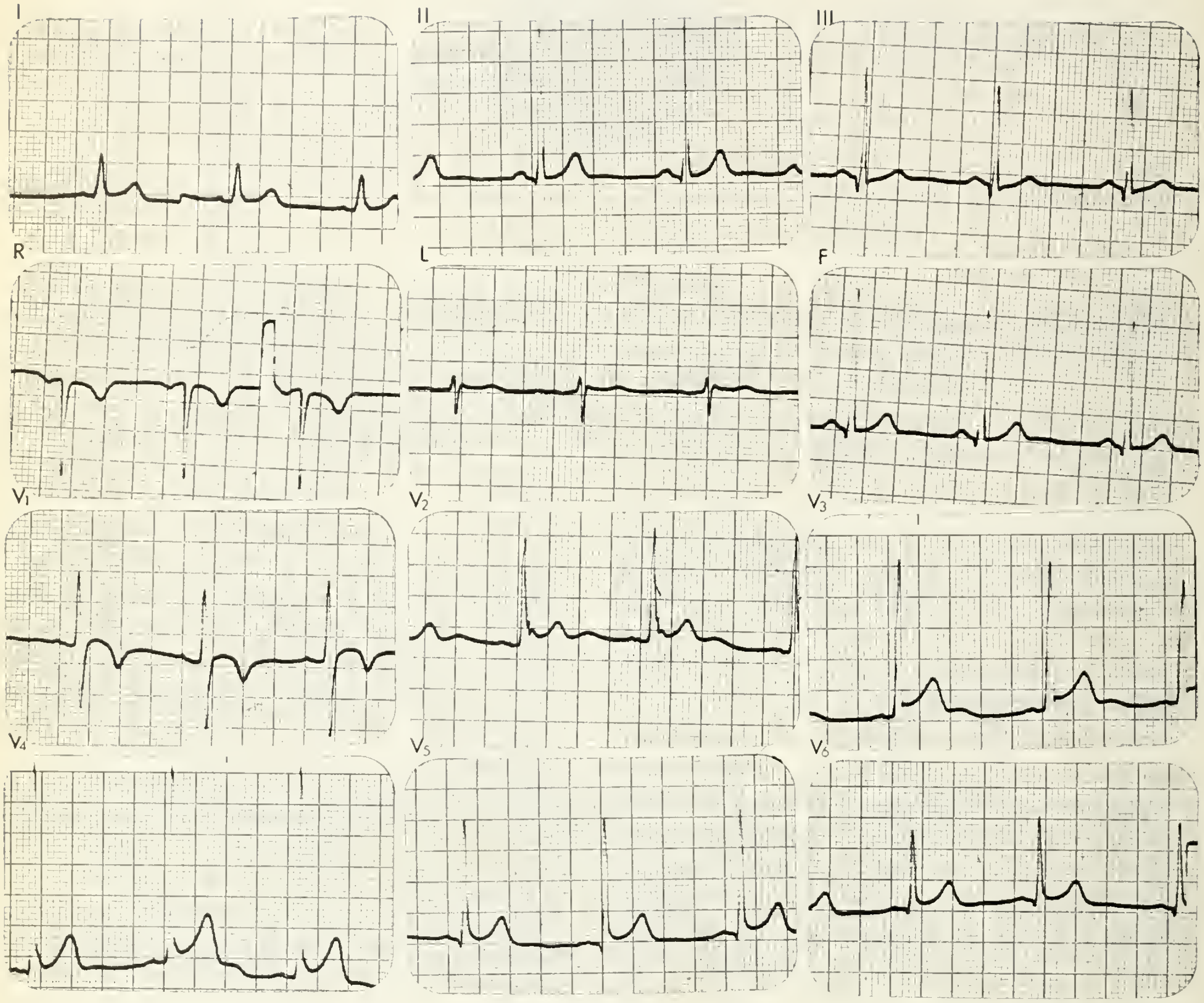

Figure 1
Black male, age 30. No clinical evidence of heart disease.

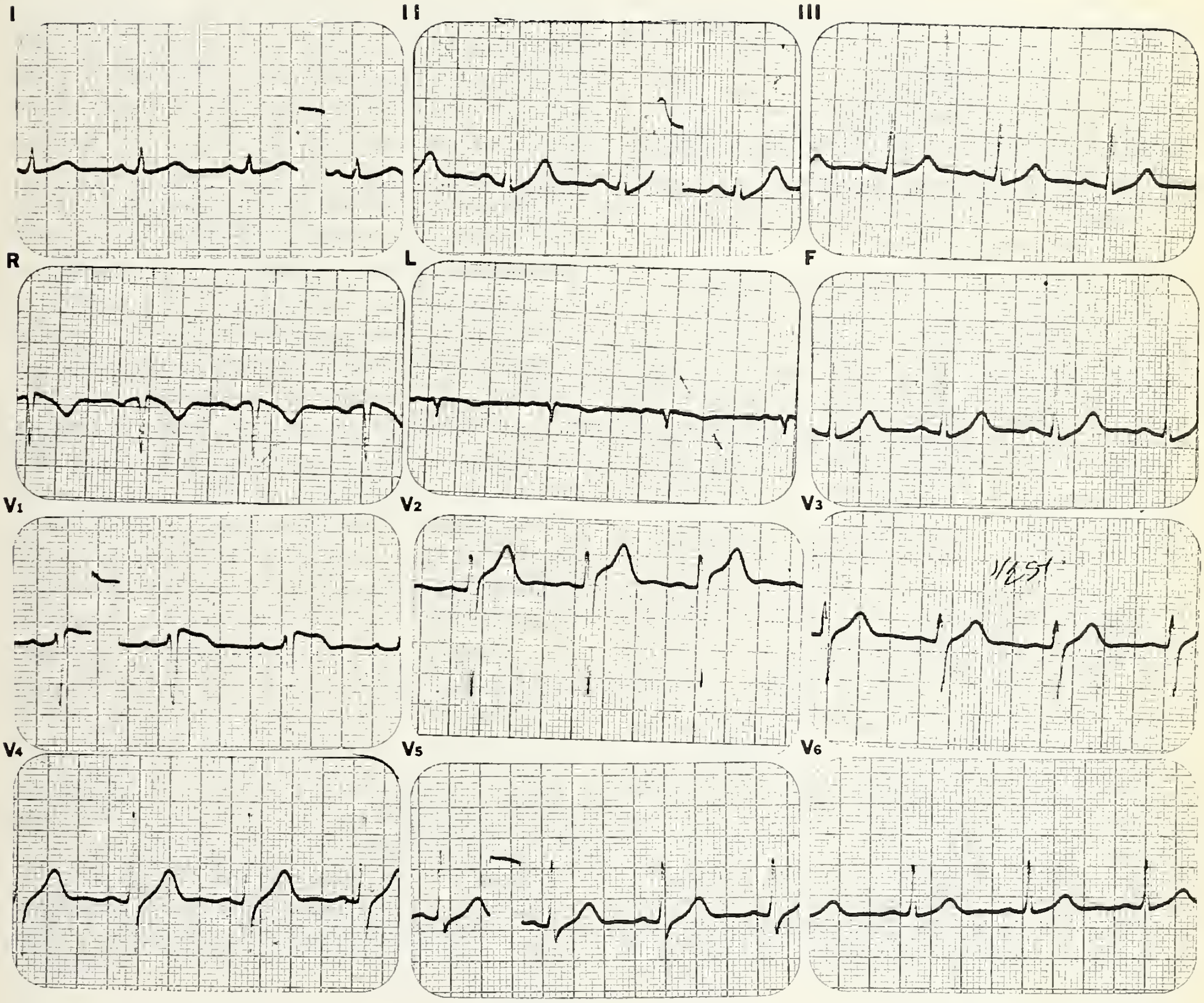

Figure 2
Black male, age 20. No clinical evidence of heart disease.

OBITUARIES

Harold D. von Glahn, M.D.
1915-1972

Dr. Harold D. von Glahn of Ferry Road, Old Lyme, died in Lawrence and Memorial Hospital, New London at the age of 57.

Dr. von Glahn was engaged in private practice in Old Lyme for the past 25 years.

He was a graduate of Duke University and the Duke University Medical School. He was a member of Sigma Phi Chi Medical and Sigma Phi Epsilon fraternities.

Dr. von Glahn was a member of the Connecticut Medical Examining Board, having first been appointed in January, 1964 by former Governor John Dempsey and was reappointed in December, 1968.

He was a past president of the Connecticut Academy of General Practice, past president of the American Academy of General Practice, first chief of general practices at Lawrence and Memorial Hospital and a member of the present general practice staff at the hospital.

He was also a member of the National Board of Medical Examiners, the American Geriatrics Society and the Royal Society of Health of England and the Thames Club of New London.

Dr. von Glahn was a member of the American Medical Association, Connecticut State Medical Society, New London County Medical Association and was Associate Councilor from the New London County Medical Association.

He leaves his wife, Edith Lambot von Glahn; a son, Peter, a senior at Jamestown College, Jamestown, North Dakota; a daughter, Mrs. Burton Mousch of Old Saybrook; and a sister, Mrs. Dorothy Fils of Ossining, New York.

Clifford E. Wilson, M.D.

George Harold Gildersleeve, M.D.
1898-1971

Dr. George H. Gildersleeve, retired Chief of the Surgical Service and a past president of the Medical Staff of the William W. Backus Hospital, Norwich, and Medical Examiner for Norwich, died December 22, 1971.

Dr. Gildersleeve was born in East Woodstock, Connecticut on June 16, 1898, the son of the late Charles C. Gildersleeve, M.D., and Susan Corbin Gildersleeve. He graduated from the Norwich Free Academy, received a Ph.B degree from Brown University, Class of 1919, and his medical degree from Yale University School of Medicine in 1923. His internship was spent at Hartford Hospital. He served in the United States Navy during World War I and remained in the Naval Reserve until 1921.

He began his practice in Norwich in 1925 and limited it to general surgery in 1948. His personality and medical skill won the deep admiration and respect from all associated with him. He was elected a member of the American College of Surgeons on October 16, 1931, was a fellow of the Academy-International of Medicine, a member of the New London County Medical Association, a member and past president of the Connecticut State Medical Society, the American Medical Association, the Yale Medical Alumni Association and the Hartford Hospital Alumni Association. He held the position of consulting surgeon to the Uncas-on-Thames and Norwich Hospital.

Dr. Gildersleeve not only served his profession with highest dedication but also served his community with distinction. For over thirty years he was associated with the Connecticut Public Health Council, Committee on Aging of the Connecticut State Medical Society, was a director of the Board of Chelsea Savings Bank of Norwich as well as serving as its vice-president. He was a member of the Robert O. Fletcher Post of the American Legion, a past deacon of the Central Baptist Church and a member of the Commerce Club of Norwich.

He was a well trained and disciplined practitioner of his profession. His vast experience and knowledge were always available to patients and to fellow physicians. He possessed the ability to perform the most complicated surgical procedure with the humility he always exhibited throughout his personal life. His loss will be deeply felt by all associated with him.

He is survived by his wife, Eleanor Shumway Gildersleeve.

David Sussler, M.D.

In Memoriam

Bodie, John A., Tufts Medical School, 1924. Dr. Bodie was a general practitioner in the New Haven area since 1924. A member of the staff of the Hospital of St. Raphael, Dr. Bodie served as its president in 1956. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Bodie died January 6, 1972, at the age of 73.

Cogswell, Eliot S., Harvard Medical School, 1911. Dr. Cogswell was a radiologist in the Hartford area since 1912. He had been head of the X-ray department at University McCook Hospital and medical director of the Fuller Brush Company for many years. He retired in 1971 after 57 years as a doctor. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Cogswell died January 20, 1972, at the age of 86.

Giorgio, Nicholas A., Long Island College & Hospital, 1925. Dr. Giorgio was a pediatrician in the Hartford area since 1925. He was an Army veteran of World War I, a member of the Hartford County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Giorgio died January 5, 1972, at the age of 73.

Kennedy, Charles S., Georgetown Medical School, 1930. Dr. Kennedy was a practicing physician in the New Haven area since 1931, and a former Naugatuck health officer for eight years. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Kennedy died January 20, 1972, at the age of 69.

Markoff, Abraham, Long Island College of Medicine, 1932. Dr. Markoff was a practicing proctologist in the New Haven area since 1933. During World War II he served in the Army in the China, Burma and Indian Theater of Operations and attained the rank of captain. He was a member of the New England Proctological Society, the New Haven Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Markoff died January 16, 1972, at the age of 64.

Rockwell, Alice E., Johns Hopkins University, 1921. Dr. Rockwell, who is believed to have been the first woman to practice medicine in Bridgeport, was a practicing physician in that area since 1936. Following graduation from Johns Hopkins, Dr. Rockwell was sent by the Rockefeller Foundation to the Peking Medical Institute in China, where she interned and served as assistant resident in medicine. She was a member of the Fairfield County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Rockwell died in Minnetonka, Minnesota, January 14, 1972, at the age of 77.

NEWS
from County Associations

New Haven

New Haven County Medical Association
Annual Report of the Board of Governors

The Board of Governors met on December 2, 1971 and on January 20, 1972 and will meet again on March 2, 1972.

During these meetings the following matters were acted upon:

The principle of "open staff" hospital privileges for all qualified physicians in all hospitals was reaffirmed. Three physicians applying for privileges at the Yale-New Haven Community Hospital were strongly supported by the Board of Governors, along with the New Haven Medical Association and the Connecticut State Medical Society.

One member of the Association was reprimanded for failing to observe proper medical ethics.

Thirty-five new members were indoctrinated into Active Membership at the December 2, 1971 meeting. They were: Doctors Bradford, Dann, Farber, Garber, Gillian, Goodrich, Kundargi, Lecker, Neville, Pardi, Silva, Silver, Samore, Sonana and Roe, all from New Haven; Doctors Kostecki, Loyer, Robitaille, Eisen, Shahnazarian, Tremaglio and Piscatelli, all from Waterbury; Doctor Brown from Seymour, Doctor Langner from Southington; Doctors Lawson and Meyerson from Derby; Doctors Knowlton, Lowry and Mickenberg from North Branford; Dr. Naiman from Milford; Dr. Saracco from Hamden; Dr. Spicuzza from Woodbridge; Dr. Zelson from Orange, and Doctors Dearborn and Hourihane from West Haven.

The Board of Governors depends heavily on its various committees (30) for carrying out its business, and their actions are duly recorded in the annual committee reports. The Board is grateful to these committees and their chairmen.

The Executive Committee has met three times since the last meeting, has met twice with the Chiefs of Staff of the hospitals in the county, and also has met once with the Presidents and Vice-Presidents of the seven other county medical associations in the State.

The Councilors, Doctors Kurt Pelz, James H. Root, Jr., and Jerome Freedman have performed well as our representatives on the Connecticut State Medical Society Council, as has Dr. Louis Backhus, Connecticut State Medical Society Secretary.

Respectfully submitted,
William L. West, M.D., *Clerk*

New Haven Country Medical Association
Annual Report of the Clerk

The New Haven County Medical Association, over the past several years, has been undergoing a metamorphosis.

The Himler-Budd Report of the A.M.A. signaled the beginning. The New Haven County Medical Association and the Connecticut State Medical Society played an important role in the *changes* wrought in that report when it was finally adopted by the A.M.A.

Older physicians recall "1984" by Orwell and younger physicians recall "Future Shock" by Toffler in their awareness that some sort of change is coming and adaptation is needed.

"Change" is in the air and the Board of Governors of the New Haven County Medical Association is responsive to the fact that *"change"* is not only inevitable but is proceeding at an "exponential rate" these days.

Involvement of our members in many areas of Association action is at a high level (over 300 doctors.) Involvement of our Association in the community is beginning to increase, as is involvement in hospital and third party areas.

The concept of acting as a "group" rather than as "individuals" is gaining acceptance, and we are now one of the "groups" involved in community health planning in our county.

The year 1972 offers the members of the New Haven County Medical Association their best chance in a long time to function as a "group" amongst "other groups" in approaching some of the health problems of all of the people who live in New Haven County.

Respectfully submitted,
William L. West, M.D., *Clerk*

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Letters To The Editor

Members of the Society are invited to communicate with the Editor of CONNECTICUT MEDICINE expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all correspondence will be subject to the usual editing and possible abridgment. Material should be typewritten double spaced, and be of reasonable length (not over 1½-2 pages). Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

To the Editor:

In recent months very creditable observers have brought to public attention the matter of acupuncture as witnessed by them on visiting Red China. Their plea was not to denigrate, on the contrary, to urge serious scientific study.

American-trained physicians see no conflict with empiricism in the areas of counterirritation, psychosomatic phenomena, and the experiences of devotees of Yoga, the effect of the will as in autohypnosis, and such. Is there something we have missed in our rapid centrifugal expanses of research? Is there something to grab onto from an electro-chemical-physical standpoint which defies the centrifugal distribution of nerves? Is highly disciplined man more susceptible?

I have been mystified by the peculiarities of local anesthesia in selected cases and have transiently wondered what happened and why.

I would appreciate your usual cool balanced comments and from your wide reading and interests in physiology perhaps I may learn something. Many thanks for your usual illuminating editorials on psycho-biologic social man.

Best wishes always.

Sincerely,
Samuel Climo, M.D.

New Haven, Conn.

Dear Dr. Nahum:

You made a statement in the hall of the School of Medicine a few days ago which has caused me much thought. We were talking about my recent visit in Taiwan, and in Hong Kong for presentation, for Yale-in-China, of the University Health Building to the Chinese University of Hong Kong. I remarked that the doctors, in the 3 colleges of busy students comprising the new University, told me that these students have little if any venereal disease, but do show an unusual amount of mental anxiety. You raised the question (not "which is worse") of why one must suffer from either condition in this day and age.

Looking back to 1890, we find Sir John Simon saying in English Sanitary Institutions,"—that to procure for the life and happiness of the nation the utmost possible Freedom from Interruptions by Disease is a task well worthy to engage the best energies of many best minds, are considerations which members of my profession may well contemplate with peculiar gladness."

Many of us are concerned about the continued rise of incidence of syphilis and gonorrhea, especially among young people. And having been a member of a small national committee on Prophylaxis before WW II, and having included, in numerous state and local health surveys, tested proposals for better control of prostitution, I am surprised to learn that measures in some quarters, including those in, or near, military areas overseas, resemble those of earlier days, besides the fact that health budgets in Connecticut are being curtailed.

Clement Batelli and I wrote in 1938 on Syphilis Control in New Haven,* that the control and ultimate extermination of syphilis is the frank objective of the war being waged by the United States Public Health Service and other health authorities throughout the nation. Surgeon General Thomas Parran emphasized that this difficult goal could be attained only by the cooperation of an informed public, alive to the menace of this devastating, highly prevalent disease. The most encouraging aspect of the campaign, according to John Stokes, then, was the fact that if physician and patient wisely perform their respective functions, cure is all but inevitable. Do not these same basic principles apply also to gonorrhea, and have conditions for comprehensive action changed?

Recently, my attention was directed to the inroads of venereal disease on military operations, as well as the dire effects on civil populations, while reading Napoleon's Surgeon by J. Henry Dible.† We may read, for example, that around the middle of 1799, "During this period of respite," according to Surgeon Larrey, "we were able to appreciate the advantages and disadvantages of the Egyptian climate, and indeed it was the only time at which we had any sort of happiness." We learn that the Army had established itself in camp in the vicinity of the Pyramids, when Larrey climbed to the top and cut his name there—"a boyish act shared with William Wittman who came two years later with the Grand Vizier's Army!"

To quote further, "There were other problems." The itch, gout and a number of diseases common in France entirely disappeared in this climate; but the free intercourse which grew up between our soldiers and the local women encouraged syphilis, and in a short time there were many men in the hospital with this disease—"the immoderate use of spirits and of women." It was far from easy to prevent its spread, for to deprive the seasoned soldier who had recovered his strength and vigour of the society of women was to engender boredom and homesickness." A civil hospital was set up for the prostitutes, and also for women of this class who were pregnant, "so as to prevent the abortion which they commonly induced and to ensure the survival of their children."—A vigorous inspection was instituted in the barracks and all, suffering from venereal disease, were sent to the military hospitals and detained until they were cured. Also, "ophthalmia" was serious.

Of many plagues of Egypt, "this disease of the eyes is one which over the centuries has caused untold suffering, especially amongst invading armies. Generally accepted that the Egyptian ophthalmia (severely affected both the French and the British at Thistine), was trachoma, it seems clear that certain of his (Larrey's) cases were gonorrheal;" and he remarks upon a connection between ophthalmia and venereal disease in a memoir for Junior officers. His statement was that only a few persons escaped the disease during the last few months of 1797 and the early ones of 1798. Later, in 1801, when the French were cut off in the peninsula of Alexandria by the English, landing at Aboukir, "they had more than 3,000 cases in the space of 2½ months. The English suffered no less severely and at the end of 1810 there were as many as 2,317 blinded soldiers in the military hospitals at Chelsea and Kilmarnihan. So serious was the problem that the British government provided a special annual pension fund of L 100,000 for such men."

Such is life, sometimes!

Sincerely,
Ira Hiscock

P.S.

Soviet Minister of Public Health announced that the government has reopened a network of specialized clinics to combat an apparent resurgence of venereal disease in the Soviet Union. Previously, Soviet officials had imposed stiffer penalties—up to five years imprisonment—against persons who knowingly infect others; and had made subject to criminal prosecution those who refuse treatment or knowingly expose others. A.M.A. News, Jan. 24, 1972.

* Yale Journal of Biology and Medicine, March 1938.

† William Heineman Medical Books, Ltd, London 1970, printed by the Whitefriars Press Ltd London and Trowbridge.

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Approach to the Medical Care of the Sick Newborn. Sophie H. Pierog and Angelo Ferrara. The C. V. Mosby Company, St. Louis, 1971. 281 pp. with 42 illustrations. $11.50.

Lasers in Medicine. Leon Goldman, M.D. and R. James Rockwell, Jr. Gordon and Breach, Science Publishers, Inc., New York, 1971. 382 pp.

Statistics in Biology. Statistical Methods for Research in the Natural Sciences. Volume Two. C. I. Bliss, Biometrician, The Connecticut Agricultural Experiment Station; Research Associate, Yale University. McGraw-Hill Book Company, New York. 612 pp.

Eye Symptoms in Brain Tumors. Alfred Huber, M.D. Second Edition. Frederick C. Blodi, M.D., Editor and Translator. The C. V. Mosby Company, St. Louis, 1971. 362 pp. with 233 illustrations. $32.50.

The Pediatric Nurse Practitioner. Fernando J. deCastro, M.D., M.P.H. and Ursula T. Rolfe, B.A., M.D. The C. V. Mosby Company, St. Louis, 1972. 142 pp. $6.50.

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Iron-Fortified Formulas For Infants

Iron-deficiency anemia is common in infants and pre-school children, especially among the poor. One study of children between the ages of six and 23 months in low-income urban families showed that in almost half the hemoglobin concentration was less than 10 Gm/100 ml (M. F. Gutelius, Amer. J. Public Health, 59:290, 1969). Such anemia is usually due to a deficiency of iron in the child's diet; even the most severe depletion of iron stores in the mother during pregnancy does not cause iron deficiency in the offspring. Full-term infants are usually born with sufficient stores of iron to prevent anemia during the first months of life. Iron-deficiency anemia is less frequent after the first years, since in older children iron requirements are reduced and there is increased use of meat, eggs, and other foods that supply iron.

Effects Of Iron-Deficiency Anemia

Irritability, anorexia and listlessness are common symptoms of iron-deficiency anemia. Other disorders associated with iron deficiency include impaired absorption of vitamin A and xylose, gastric achlorhydria, and mild blood loss. Whether the gastrointestinal bleeding sometimes found in iron-deficient children is caused by iron deficiency or by intolerance to whole milk (M. E. Lahey and J. F. Wilson, J. Pediat., 69:339, 1966) is a subject of controversy. There is no evidence that iron deficiency interferes with linear growth.

Recommendation Of The American Academy Of Pediatrics

The Committee on Nutrition of the American Academy of Pediatrics recently urged that infants be fed iron-fortified milk until at least 12 months of age to prevent iron-deficiency anemia (Supplement to the Newsletter of the American Academy of Pediatrics, December 15, 1970). Some proprietary milk formulas contain little iron, and the Committee suggests that these be fortified with iron. The Committee also recommends that iron-fortified whole or evaporated milk be made available for infant feeding, but the addition of iron to whole milk is not feasible, since it hastens the development of rancidity and imparts an objectionable color change when the milk is used for cooking or coffee. Fortification of evaporated milk is being considered by manufacturers but fortified evaporated milk is not available now.

In practical effect, the Committee on Nutrition is recommending the use of fortified proprietary formulas throughout the first year of life, and manufacturers of these formulas have used the Committee's statement in promotional literature circulated to pediatricians. Normal infants who were not born prematurely do not need iron supplements during the first months, however, and most children in middle-class families eat foods that supply adequate amounts of iron and never require supplementation. When extra iron is needed it can be supplied in oral iron preparations or iron-rich foods.

Iron Requirements And Sources

Full-term infants whose diets provide 1 mg/kg/day of iron usually maintain normal hemoglobin concentrations; premature infants may need 2 mg/kg/day for several months. Non-fortified cow's milk contains only about 0.5 mg per liter and human milk 1.5 mg per liter (Committee on Nutrition, American Academy of Pediatrics, Pediatrics, 43:134, 1969). Sufficient dietary iron becomes available as soon as the infant begins to eat meat, egg yolks, and iron-fortified cereals.

Infant cereals contain 14 to 28 mg of iron per dry ounce (10 to 12 tablespoons or 120 to 180 cc of reconstituted cereal). These cereals are usually included in the infant's diet only during the first few months, however, and are not widely used at any time by the families whose children are most likely to be iron-deficient; the problem is not their cost (1 to 2¢ a day), but rather that whole milk is the food of tradition and convenience. Furthermore, the need for dietary iron in infancy and its availability in infant cereals is not widely known. Proprietary milk formulas that have been fortified with adequate amounts of iron (7.5 to 17 mg per liter) are used even less than cereals by low-income families.

Prevention Of Iron Deficiency

Medical Letter consultants doubt that the advice of the Committee on Nutrition that iron-fortified milk be used throughout the first year of life will be effective in preventing iron-deficiency anemia. Iron-fortified milk formulas, like iron-enriched cereals, will be given mostly to children of higher-income families who already have adequate dietary sources of iron. The cost of milk from proprietary formulas that are ready-to-use (and therefore as convenient as container milk) ranges from 69¢ to 89¢ per quart (in large cans; preparations sold in bottles and small cans are more costly). The concentrates cost less but are still expensive (about 43¢ to 48¢ per reconstituted quart). Pasteurized whole milk costs 31¢ to 35¢ per quart, and reconstituted evaporated milk costs about 22¢ per quart.

Reprinted from *The Medical Letter on Drugs and Therapeutics,* New York, N.Y., Vol. 16, August 6, 1971.

Connecticut Medicine

MANUSCRIPTS

Manuscripts, including references or bibliography, must be typewritten, double-spaced on white paper 8½ x 11 inches with adequate margins on firm paper. The original copy, not the carbon copy should be submitted. Carbon copies or single spaced manuscripts will not be considered. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Receipt of manuscripts will be acknowledged and unused manuscripts returned. *Accepted* manuscripts become the permanent property of the Journal and may not be reprinted elsewhere without permission from both the author and Connecticut Medicine. The author is responsible for all statements made in his work, including changes made by the copy editor.

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STYLE

The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the Journal (listing name and initials of author, title of article, Journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

ILLUSTRATIONS

Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration as well as typed on a separate sheet. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. Connecticut Medicine will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

NEWS

Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

ADVERTISING

All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by Connecticut Medicine.

Material other than original articles should be received not later than the 10th of the month PRECEDING date of issue.

REPRINTS

Reprint orders should be returned at once as the type will be destroyed immediately following publication of the manuscript. The Journal does not stock reprints of the articles published. Requests for individual reprints should be sent to the author.

Communications should be addressed to Louis H. Nahum, M.D., Editor, Connecticut Medicine, 160 St. Ronan Street, New Haven, Conn. 06511. Telephone 865-0587.

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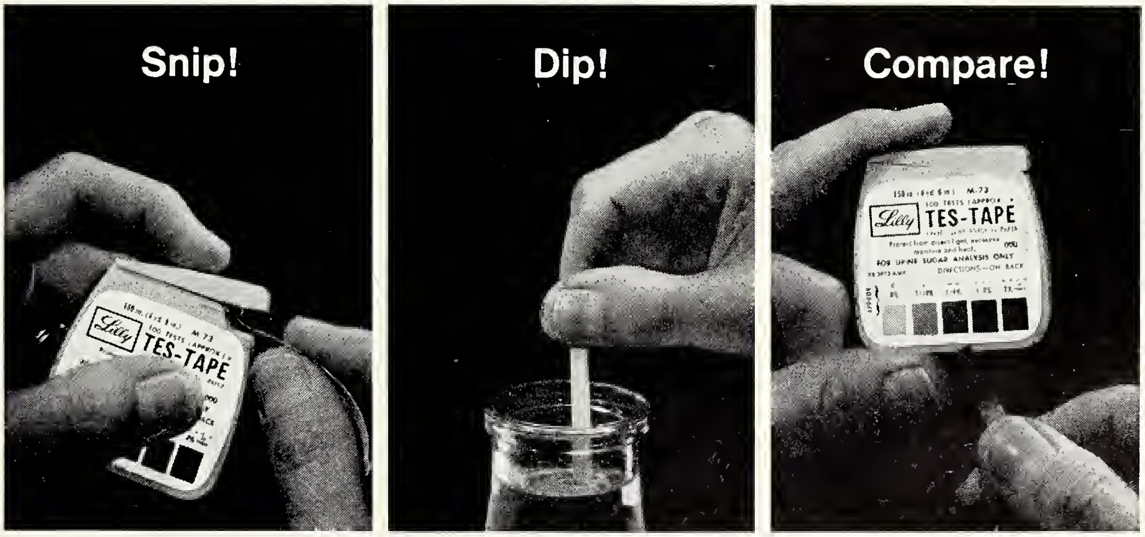

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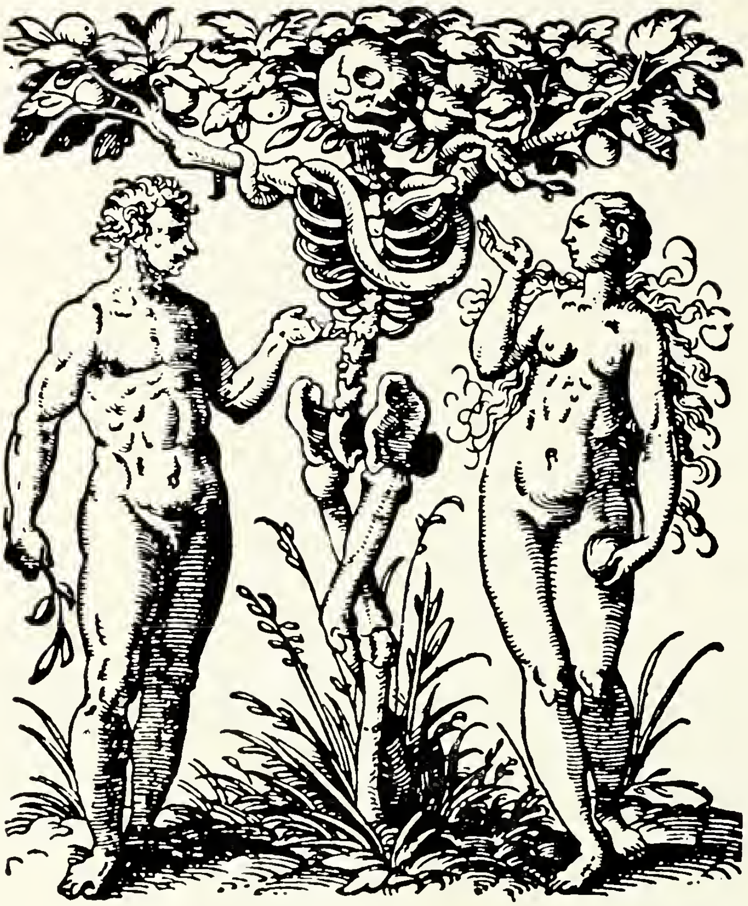

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Contraindications: Contraindicated in patients previously found hypersensitive to Trobicin. Not indicated for the treatment of syphilis.

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Warnings: Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

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*Data compiled from reports of 14 investigators. **Diagnosis was confirmed by cultural identification of *N. gonorrhoeae* on Thayer-Martin media in all patients. Criteria for cure: negative culture after at least 2 days post-treatment in males and at least 7 days post-treatment in females. Any positive culture obtained post-treatment was considered evidence of treatment failure even though the follow-up period might have been less than the periods cited above under "criteria for cure" except when the investigator determined that reinfection through additional sexual contacts was likely. Such cases were judged to be reinfections rather than relapses or failures. These cases were regarded as non-evaluatable and were not included. JA72 1848-6

globin; hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

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PRESIDENT'S PAGE

My term of office as president of the Connecticut State Medical Society comes to an end on April 25. It has been a year in which I have had the opportunity to visit the County Associations on the occasion of both their semi-annual and annual meetings; attend the annual meeting of the Medical Society of the State of New York; and attend two sessions of the AMA House of Delegates. Listening to the discussions at these meetings is very informative. The major concern at all of them revolved around the problem of accommodating medical practice to the changes already brought about by health care legislation and planning methods to meet the expectation of future government intervention. This was true whether the meetings were at the AMA level, dealing with national problems, or at the county associations level, trying to adjust to local and state statutes and regulations.

I was most impressed during these hours of listening with the need to keep communications open all the way down to the individual practitioner. He must know what is going on and he cannot be left out of the educational process in socio-economics anymore than he can neglect keeping up to date in scientific advances.

The AMA provides news in the political and economic field in the JAMA, in the weekly Legislative Roundup published by the Council on Legislation, the AMPAC publications, and probably most completely in American Medical News.

The State Society has a variety of publications to keep members up to date on local activities: Connecticut Medicine with special communications occasionally enclosed in it, Connecticut M.D., and Political Roundup. The Society makes a considerable effort to get many types of news to its members.

Sources other than those within the organization are equally important. The newspaper must be looked through daily, otherwise an important item may be missed. Magazines of all kinds usually include some medical article which ought to be perused if only to see the point of view taken by the editor and his "message" to his readers.

The information from all these communications should stimulate thought on the part of the individual which he can bring to the organization (county, state, or national) in the form of ideas, new concepts, and points of view as his contribution.

As I sit in on meetings, I never fail to be impressed by the evolution of an idea brought forth by one person, discussed by several others and modified, changed, accommodated to include facts considered important by others, and finally evolve as a program, all as a result of communications flowing freely between individuals all seeking a common goal.

To stimulate these ideas you must read or scan all the material you can get your hands on. Then discuss your thoughts with others at the earliest opportunity before your impressions cool off. If you have suggestions you want considered by your county association, you have only to go to the meeting and express yourself. If you want your thoughts brought to the State Society, communicate with your delegate and it can be acted on at the House of Delegate sessions. This is the last opportunity for me to communicate my ideas to you on this page. I hope they will stimulate you to transmit ideas of your own. They will be welcome.

It has been a great honor and a gratifying experience to serve as your president during the past year for which I am humbly grateful. I am proud to commend to you your president for the ensuing year, David A. Grendon, M.D., for whom I have the highest respect and in whom I know the Connecticut State Medical Society will find a great leader.

Frederick C. Weber, Jr. M.D.

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A Psychiatric Unit for the short term patient has opened at New Lakeview Convalescent Home, an ECF in Cheshire. Staff and consulting psychiatrists work with specialized staff members to provide highly individualized treatment programs—the rates for this service are set at a moderate level for the patient. Medical problems are under the direction of a physician devoting time exclusively to this 30 bed unit. The Home is accredited by the joint commission on accreditation of hospitals. New Lakeview a 210 bed facility, is set in the country overlooking a lake and is located at 50 Hazel Drive, Cheshire. Further information can be obtained from Mr. Stephen Potash, Administrator, at 272-7204.

Hyperglycemia and Insulin Resistance During Glucagon Infusion

Bruce A. Chabner, M.D., Stuart J. Brill, M.D. and Philip Felig, M.D.

Introduction

The hyperglycemic action of the polypeptide hormone glucagon has been known for many years. Recently this agent has attracted attention as an inotropic drug in the treatment of congestive heart failure and cardiogenic shock.[1] Despite its potent metabolic actions, to date few side effects, other than nausea and vomiting, have been reported to attend the use of glucagon when given as an intravenous infusion or bolus.[2] Recently, Nord *et al.* noted the development of marked hyperglycemia without ketoacidosis persisting throughout a period of glucagon infusion in an insulin-dependent diabetic.[3] In the patient to be described, marked hyperglycemia, hyperosmolarity, and insulin resistance accompanied the infusion of glucagon for treatment of cardiogenic shock. This case report as well as other clinical and experimental evidence suggests that intravenous glucagon should be used with caution in diabetic patients if serious disruption of glucose homeostasis is to be avoided.

Report of a Case

A 72 year old woman entered the hospital because of chest pain. Eight years prior to admission, diabetes mellitus had been diagnosed; for six years she was treated with oral hypoglycemic agents. Two years prior to admission oral agents were discontinued, and treatment with isophane (NPH) insulin was begun at a dose of 50 units each morning and 10 units each evening. Glycosuria was noted intermittently thereafter, but there were no episodes of keto-acidosis or symptomatic hypoglycemia.

For the five years prior to admission the patient had experienced several attacks of angina pectoris each day. At 1:30 a.m. on the night of admission she awoke with severe substernal chest pain and was rushed to the hospital. On arrival, she was diaphoretic and obtunded, with a blood pressure of 50/0. The pulse was 84 and regular. Temperature and respiration were normal. The extremities were cool. The eyes, including fundi, were unremarkable. Neck veins were distended at 30° elevation. The cardiac impulse was not felt and the heart sounds were faint. A firm liver edge was felt four fingerbreadths below the right costal margin. There was no abdominal tenderness. There was a trace of pertibial edema.

Results of laboratory tests included: White blood count 11,800 per cm^3 with normal differential, BUN 21 mg/100 ml, plasma glucose 604 mg/100 ml; serum sodium 130, potassium 3.3, chloride 99, and bicarbonate 14.2 mEq/l. Serum amylase was normal. The ECG showed a normal sinus rhythm with occasional atrial premature beats and nonspecific ST-T wave changes. Chest X-ray revealed cardiomegaly with clear lung fields.

The clinical diagnosis was acute myocardial infarction with cardiogenic shock. An intravenous infusion of isoproterenol (Isuprel) was begun, blood pressure rose to 110/0 and the patient became alert. Because of the hyperglycemia, 15 units of regular insulin were administered intravenously. The patient's condition remained stable, with good urine output until four hours later, when she suffered a cardiac arrest. Resuscitation efforts were successful; with the aid of intravenously infused isoproterenol (2-8 μg/min), and glucagon (5 mg/hr), a blood pressure of 120/60 and pulse of 112, were restored. However, the plasma glucose two hours after beginning the glucagon infusion was 1000 mg/100 ml. Urine acetone was small and serum acetone negative. Blood pH was 7.45. Despite a total of 600 units of regular insulin administered intravenously in doses of 50-100 units at hourly intervals, the plasma glucose remained over 1000 mg/100 ml for the next ten hours, and serum osmolality reached 334 mOsm/l. At this point the intravenous infusion of glucagon was discontinued leaving Isuprel as the sole inotropic agent. Over the next 11 hours plasma glucose declined to 384 mg% following administration of 300 additional units of regular insulin. A repeat serum osmolality was 306 mOsm/l.

During the second hospital day, the plasma glucose remained between 300 and 400 mg% with the use of no additional insulin. The patient remained alert but hypotensive until 48 hours after admission when she suffered a second cardiac arrest. Resuscitation was unsuccessful. Autopsy permission was refused.

Discussion

In the initial reports of the clinical use of glucagon as an inotropic agent the side-effects noted were nausea and vomiting,[2,4,5] and a decrease in serum calcium,[2] and potassium.[5] Despite the use of doses far in excess of physiologic levels, only mild

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elevations of blood glucose were observed (never greater than 200 mg/100 ml) in response to bolus injection or continuous infusion of glucagon.[2,7] However, a recent report[3] has briefly called attention to the development of marked hyperglycemia in a single patient with insulin-dependent diabetes. In the present case, similar metabolic problems were encountered; severe hyperglycemia and hyperosmolality persisted throughout a 12 hour period of glucagon infusion despite massive doses of intravenous insulin, and were corrected only after discontinuation of the glucagon infusion.

The primary physiologic actions of glucagon relate to carbohydrate metabolism. By promoting hepatic glycogenolysis and gluconeogenesis, the hormone raises blood glucose levels. Furthermore, an important role for glucagon in exaggerating the metabolic consequences of insulin lack has recently been suggested, based on the finding of relative or absolute hyperglucagonemia in patients with diabetes mellitus.[8,9]

The patient's underlying diabetes mellitus and hyperglycemia at the time of admission undoubtedly rendered her more vulnerable to the metabolic effects of glucagon. Crockford et al have demonstrated an increased sensitivity to the hyperglycemic effects of glucagon in diabetic patients.[10] While the acute catastrophic illness suffered by this patient would of itself disturb diabetic control, the ease of restoration of control with discontinuation of glucagon despite the persistence of cardiac failure suggests that glucagon played a central role in the observed metabolic derangements. Fortunately, the more dangerous problem of diabetic keto-acidosis was not encountered in this case and has not been reported in conjunction with the use of intravenous glucagon. However, the potential metabolic hazards of glucagon infusion should be recalled when this drug is used in the treatment of refractory heart failure, particularly in patients with insulin-dependent diabetes.

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Permanent Ventricular Pacing Through The Coronary Venous System

Report of Two Cases and Review of the Literature

J. M. Kabemba, M.D., J. A. Ogden, M.D. and J. Atocha, M.D.

Synopsis-Abstract

Two cases of long term ventricular pacing through the coronary sinus are presented. Ten cases have been previously reported. In most instances the catheter was inadvertently placed in the coronary sinus. Chronic pacing has been satisfactorily achieved in our two cases. Threshold levels, electrocardiography, lateral chest X-ray, or biplane fluoroscopy appear to be diagnostic indicators for this unusual location.

Transvenous endocardial pacing of the heart for heart block has virtually replaced direct electrode implantation by thoracotomy. With the exception of a few cases, such as congenital heart block in children, major thoracotomy for pacemaker insertion is no longer necessary. However, some problems have arisen from use of the transvenous route: Perforation of the right ventricle, bacterial endocarditis, poor contact between the tip of the catheter and the right ventricular wall with subsequent failure to pace, and placement of the electrode in the coronary venous system instead of the apex of the right ventricle.

Placement of the catheter in the coronary sinus may occur any time during the insertion of a transvenous pacemaker. During the pacemaker implantation, fluoroscopy is routinely employed, but in most instances it is confined to frontal projection. Under these circumstances, one can not be certain about the location of the tip of the electrode. The purpose of this study is to report two cases of permanent pacing through the coronary sinus, to review the literature, and to discuss recognition of this unusual site at the time of initial insertion.

Case Report 1: F. L.

This 76 year old man was admitted to the hospital on April 13, 1969 with a history of shortness of breath, congestive heart failure and several episodes of syncope. He was a heavy smoker (2-3 packs a day) and had been treated for hypertension for the previous two years.

On admission the pulse rate was 36 per minute, the B/P was 190/100 and the respiratory rate was 26 per minute. There were rales heard over his entire chest. No cardiac murmur was heard. The plain chest X-ray showed left ventricular enlargement and bilateral pleural effusion. The electrocardiogram showed left bundle branch block and second degree heart block (Fig. 1). On April 24, 1969, an endocardial, demand type pacemaker (Medtronic) was implanted. The catheter was inserted via the basilic vein. The patient was then paced constantly at a rate of 60 per minute (Fig. 2). His threshold was 1.5 ma. An A.P. chest X-ray obtained before the conclusion of the procedure was interpreted as showing the catheter tip in the apex of the right ventricle (Fig. 3). But lateral films, taken post-operatively, showed the tip of the catheter in a position compatible with lodgement in the coronary venous system (Fig. 4). Retrospective review of the electrocardiogram demonstrated the pacemaker impulse originating from the left ventricle, with subsequent right bundle block.

Because the pacemaker was driving the ventricles with 1:1 response, the catheter was left in the coronary sinus and the patient was discharged ten days later in good condition.

On October 22, 1970, he was readmitted for elective replacement of the pulse generator (18 months after pacing was first instituted). No pacemaker failure was observed during this period of time. The chest X-ray showed the tip of the catheter in the same position, and the electrocardiogram showed that the patient was pacing continuously with right bundle branch block. The threshold at this time was 1.5 ma. Following generator replacement he has continued on an uneventful course. It is now twenty nine months since the original implantation.

Case Report 2: L. P.

This 70 year old man was admitted to the hospital with a history of dizzy spells and syncope. His past medical history was unremarkable except for hypertension (untreated).

On admission the pulse rate was 36 per minute and the blood pressure was 150/70. No cardiac murmur was heard. The lungs were clear.

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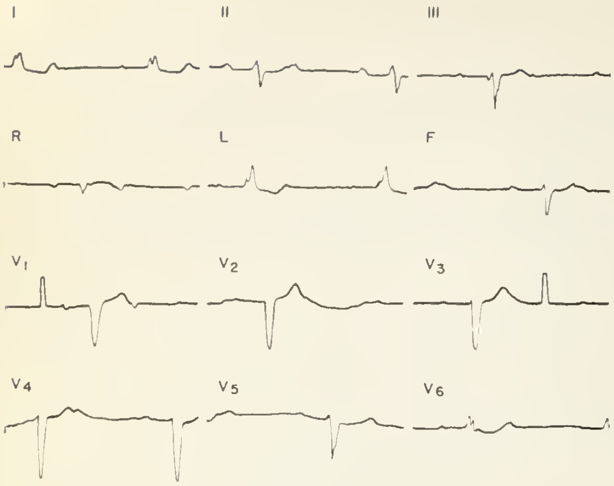

Figure 1
Preoperative E.K.G. (Case 1).

The initial electrocardiogram showed complete heart block (Fig. 5). The chest X-ray was within the normal limits.

He was treated with atropine and isuprel for several days without any improvement.

On July 24, 1970, he was taken to the operating room and with fluoroscopic control, a demand pacemaker (Medtronic) was implanted. The catheter was inserted via the basilic vein. The threshold was measured at 4 ma. The A.P. and lateral chest X-ray obtained at the end of the procedure showed the tip of the catheter in the coronary venous system (Fig 6). The electrocardiogram (Fig. 7) showed a good pacing with right bundle branch block. Because there was 1:1 response, the catheter was left in the coronary sinus. The patient paced well until the third post-operative day, when intermittent pacing was noticed and the patient complained of hemidiaphragmatic contractions for the first time. Because of this, the catheter was withdrawn a few centimeters to attempt repositioning in the apex of the right ventricle. Excellent pacing was obtained and diaphragmatic pacing disappeared. Post procedure films, however, showed the catheter was still in the coronary sinus. No further manipulation was performed. He is well fourteen months post-operatively.

Discussion

Ten cases of chronic pacing through the coronary sinus have been reported in the literature. In most of the cases, the catheter was inadvertently lodged in the coronary venous system. The duration of pacing varied from 2 weeks to 24 months.

Anagnostopoulos et al.[1] have inserted permanent catheters through the coronary sinus in two patients who developed heart block following tricupid valve replacement. Satisfactory cardiac pacing was achieved, but unfortunately both patients died of other causes 14 and 18 days after pacemaker implantation. In one patient the threshold was 1 ma; in the other, it was so high that a radio frequency pacemaker receiver was necessary.

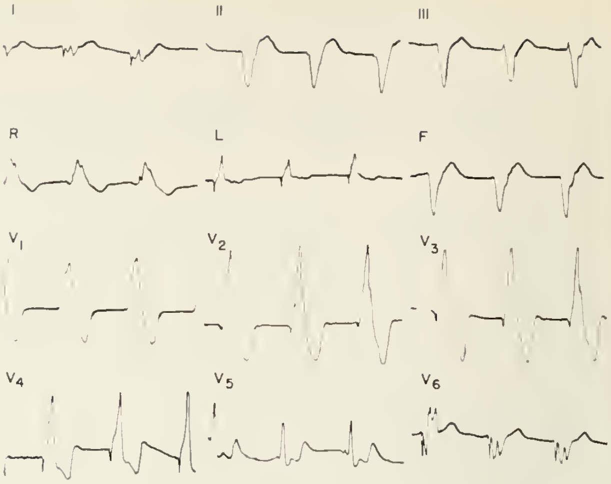

Figure 2
Post pacemaker insertion Electrocardiogram which shows right bundle branch block. (Case 1).

Castellanos[2] et. al. reported a patient who was paced for 18 months. When the patient died of cerebral hemorrhage, the pacemaker electrode was found in the coronary sinus rather than the expected right ventricle.

Meyer et al.,[3] in a review of endocardial catheter pacing, encountered five cases of coronary sinus pacing. Four of these five patients had experienced one to fourteen days of intermittent pacemaker failure and had to be returned to the operating room for reposition of the catheter in the apex of the right ventricle. The fifth patient was doing well 14 months after catheter insertion in the coronary sinus.

Culotta[4] found five patients in whom the catheter was inadvertently placed in the coronary venous system. Four of them showed good ventricular response for periods of 14, 17, 20 and 24 months. Two had persistent hemidiaphragmatic twitching and a high threshold; in each case the catheter was pulled back and repositioned in the apex of the right ventricle at the time of pulse generator replacement. The initial thresholds were respectively 0.8, 0.75, 0.8 and 0.8 ma.

Spizberg and co-workers[5] reported one case of coronary vein pacing for 18 months. The patient had early failure of his pacemaker due to a defective pulse generator, but did well following replacement. The patient died of a cause unrelated to his cardiac block. At postmortem examination, the tip of the wire was found in the middle cardiac vein near the apex of the left ventricle.

Hunt et al.[6] have also reported one case of successful coronary venous pacing for more than 16

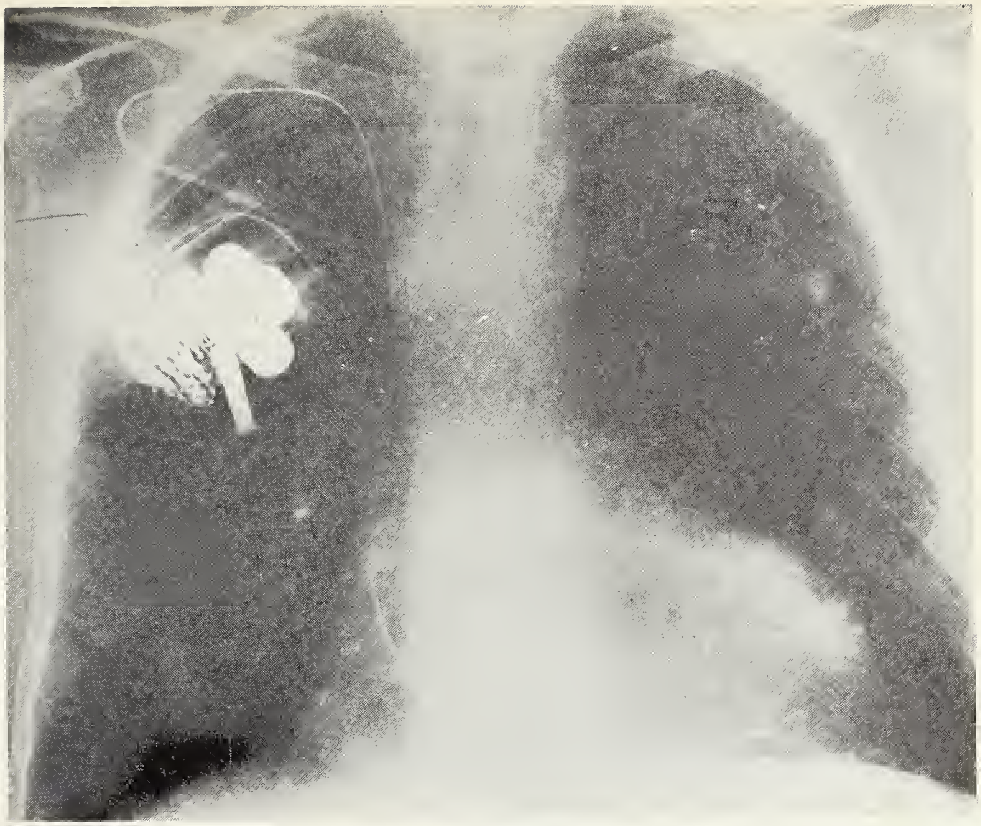

Figure 3
P.A. chest X-ray. (Case 1) The catheter seems to be in the apex of the right ventricle.

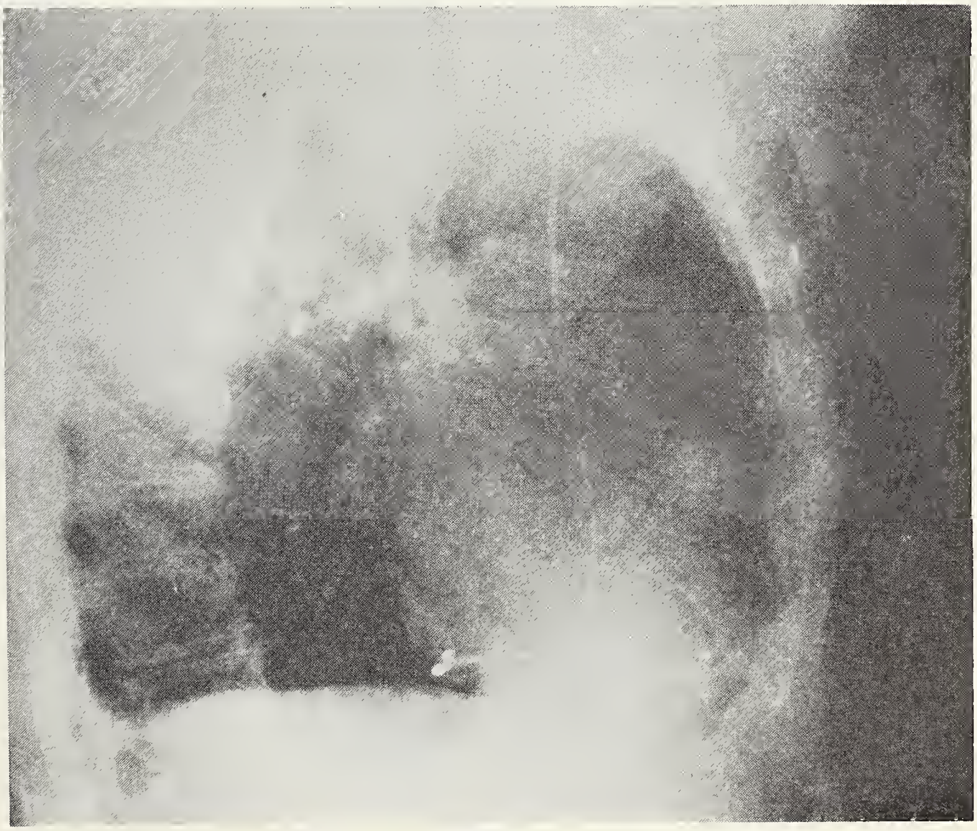

Figure 4
Lateral chest X-ray (Case 1) Showing the catheter in a position compatible with the coronary sinus.

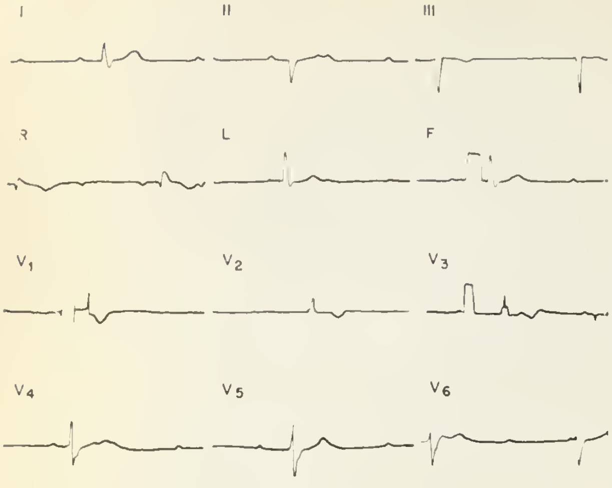

Figure 5
Preoperative electrocardiogram. (Case 2).

months. At the death of the patient, the catheter, which was thought to be in the right ventricle, was found in a tributary of the coronary sinus, behind the left ventricle.

In all these instances, except in two cases reported by Anagnostopoulos,[1] the catheter was inadvertently placed in the coronary sinus. The diagnosis was made in retrospect by electrocardiogram, lateral chest X-ray or postmortem examination.

Intentional positioning of the pacemaker wire in the coronary sinus has been used recently for treatment of arrhythmias associated with an intact atrioventricular node. In these patients atrial pacing was desired to maintain nearly normal hemodynamic and electrophysiologic relationships.[7,8]

Although the coronary sinus is an unusual site, satisfactory ventricular pacing may be obtained, as illustrated by the ten cases in the literature and the two cases reported in this paper. Placement in this structure may be recognized during the procedure by simple methods such as threshold measurement, electrocardiography, lateral chest X-ray, or biplane fluoroscopy.

Threshold Measurement

This measurement is routine in all the patients. Siddons and Sowton[9] have showed that threshold levels for ventricular pacing are usually high in the coronary venous system.

Zucker and co-workers[10] demonstrated that in dogs the electrical potential needed to pace a ventricle was only 0.25 and 0.5 volts, while much higher voltages were required to pace from the coronary sinus. Therefore malplacement of the threshold levels can be obtained by coronary sinus pacing. In one of our patients the initial threshold was 1.5 ma and remained at this level for 18 months. On the other hand it was 4 ma. in the second case. This threshold should not have been accepted.

Gulotta[1] measured threshold levels from the coronary venous system in six normal individuals. The values were found to vary significantly even in the same patient acting as his own control. He concluded that threshold levels are helpful only if high levels are encountered. Normal thresholds still require further investigation.

Electrocardiogram

There are no particular electrocardiographic features that distinguish coronary sinus pacing from endocardial pacing. Electrical pacing of the right ventricle produces an electrocardiographic pattern of left bundle-branch block.

Since a catheter lodged in the coronary sinus will usually wedge in one of its tributaries and therefore be in contact with the surface of the left ventricle, pacemaker catheter should be suspected whenever

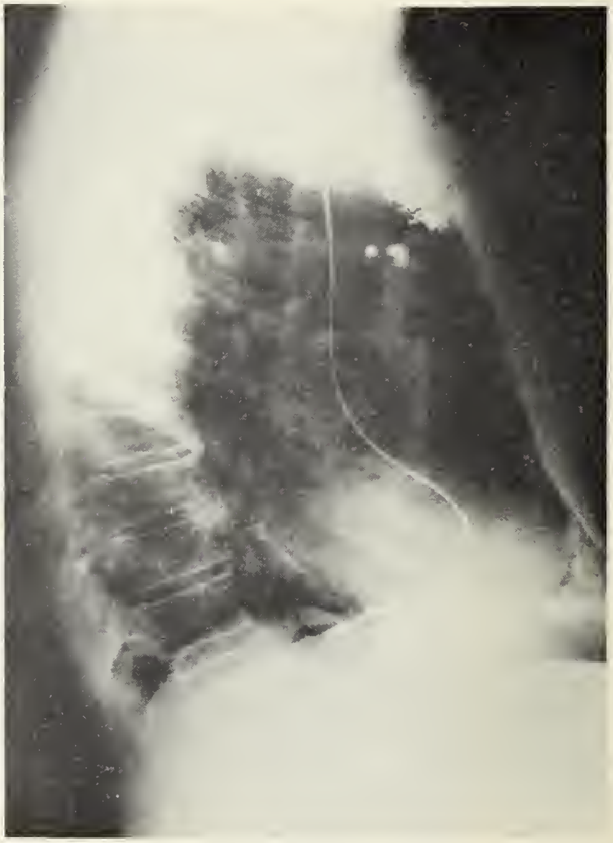

Figure 6
Lateral chest X-ray showing the catheter in the coronary sinus. (Case 2).

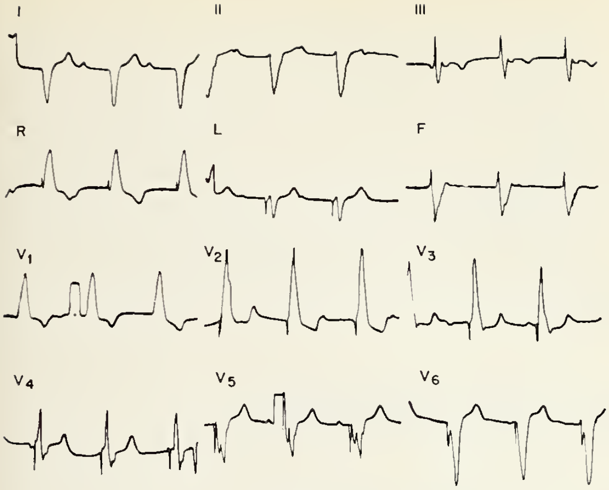

Figure 7

Post pacemaker insertion electrocardiogram with right bundle branch block. (Case 2).

electrical pacing will show electrocardiographic pattern of the right bundle-branch block, particularly in the precordial leads.

Both the cases collected from the literature and our own demonstrated a right bundle-branch block pattern suggesting that the electrical impulse stimulated the left ventricle (Fig. 2, 7). A persistent picture of right bundle-branch block with a pacemaker presumably in the right ventricle, should suggest penetration of the interventricular septum or abnormal position in the coronary sinus system. The former is very rare, while the latter is common.[2,4] A third possibility may be location of the catheter tip at the membranous septum with electrical penetration through to the left side. Right bundle-branch block pattern is suggestive of malposition of the pacemaker electrode in the coronary venous system.

Roentgenography

The routine P.A. chest X-ray and the fluoroscopy confined to the frontal projection are not helpful and will not detect the malposition. Malposition becomes apparent when lateral views are obtained.

If the electrode tip is located in the apex of the right ventricle, the lateral chest X-ray film or lateral view by fluoroscopy will show the wire lying immediately behind the sternum (Fig. 8). If, however, it is placed in the coronary sinus, the catheter will be seen pointing backward to the vertebral spine (Fig. 4, 6).

Of the three methods, roentgenography seems to be the most reliable for detecting incorrect placement of the pacemaker catheter.

Conclusion

While pacing through the coronary sinus is not a recommended procedure, a few patients have been shown to tolerate this unusual placement, indicating that, in unusual circumstances, coronary sinus pacing might be used. Such forseeable indications could be a prosthetic tricupid valve[3] or selective atrial pacing.[8,9] Before the completion of the implantation procedure, a full electrocardiogram and lateral chest X-ray (if biplane fluoroscopy is not available) should be obtained in order to recognize the desired position of the catheter.

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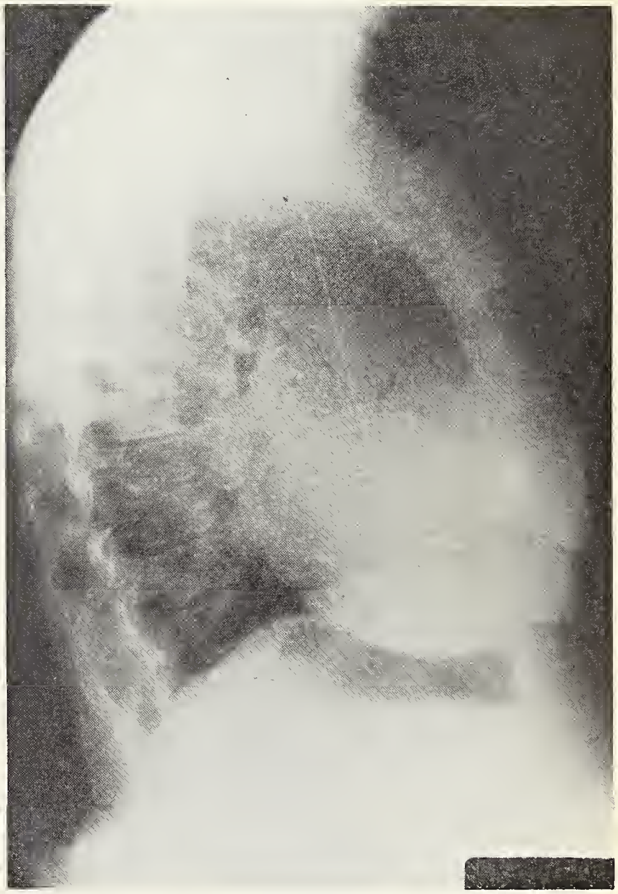

Figure 8

Correct position in the apex of the right ventricle. The tip of the catheter is pointing toward the sternum.

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Carpal Tunnel Syndrome: Diagnosis and Treatment

George E. Becker, M.D. and Carl V. Granger, M.D.

Carpal tunnel syndrome (CTS) is a common clinical entity. Although described in 1913 by Marie and Foix,[1] and others, it is only since the classic papers of Brain et al (1947),[2] Cannon and Love (1946),[3] Phalen et al (1950)[4] and Tanzer (1959)[5] that the condition has received general recognition. Nevertheless, one still encounters a number of patients with the signs and symptoms of CTS who have been mistakenly treated for cervical spondylosis, thoracic outlet syndrome, psychoneurosis, or other conditions. This indicates that many physicians who first see these patients are not recognizing the syndrome. In the thirty-three months between March 1966 and December 1968, twenty-seven patients with CTS (involving thirty-nine hands) were diagnosed in a general orthopedic practice; of these patients four (with five involved hands) had no electrodiagnostic studies and are excluded from this report. An additional three patients (with five involved hands) had electrodiagnostic studies not performed by one of the authors and for the sake of uniformity, they too are excluded. (These seven excluded patients underwent surgical release of the ten involved carpal tunnels, and have enjoyed prompt and lasting relief of symptoms.)

Four observations prompted this report: 1) CTS is common. 2) CTS is often not recognized. 3) Precise and accurate diagnosis of CTS is possible. 4) Prompt and lasting relief of symptoms can be expected following surgical release.

Abbreviations Used

CTA	carpal tunnel amplitude
CTL	carpal tunnel latency
CTS	carpal tunnel syndrome
CTV	carpal tunnel velocity
DL	distal latency
EMG	electromyogram
FV	forearm velocity
ms	milliseconds
m/s	meters per second
uv	microvolts
SL	sensory latency

Clinical Material and Methods

Twenty-nine instances of median nerve compression in twenty patients are reviewed. Of these

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twenty patients examined electrodiagnostically seventeen were women, ages 30 to 74 with an average age of 50. The three men were 19, 50 and 56 years old. Thirteen patients presented with unilateral symptoms (seven on the right, six on the left). Seven patients presented with bilateral symptoms. Most patients had had symptoms for less than a year. One patient had had anterior cervical interbody fusion at the C5-C6 level two years earlier for the same symptoms. One patient had moderate deformity of wrist and fingers secondary to rheumatoid arthritis. Another patient with prior history of rheumatoid arthritis was without deformity. No patients had had wrist fractures and none had diabetes mellitus, myxedema or other significant medical disorders.

All surgical releases were performed by one of the authors (G.E.B.). The clinical diagnosis was confirmed by electrodiagnostic studies performed by the other author (C.V.G.). Five asymptomatic patients underwent postoperative nerve conduction studies.

Electrodiagnostic examination was accomplished with commercially available electromyographic and nerve conduction testing equipment.* The median nerve was tested bilaterally. The ulnar nerve was examined if median function was impaired or if symptoms suggested ulnar nerve involvement.

Evoked efferent muscle potentials were registered by means of a coaxial needle electrode placed in the opponens pollicis muscle (Fig. 1). The position of the needle tip was adjusted to give a steep deflection at supramaximal stimulation of the nerve. (A negative initial deflection is always sought, since this indicates that the active electrode is in the region of the motor end-plates.) Conduction latencies were measured following stimulation of the median nerve (1) proximal to the elbow, (2) proximal to the wrist, and (3) in the palm distal to the transverse carpal ligament. The distances between cathodal stimulation sites were measured and motor conduction velocities calculated for both forearm and carpal tunnel.

Evoked afferent nerve potentials were registered from (1) orthodromic sensory fibers by means of surface electrodes placed proximal to the wrist following supramaximal stimulation of the index and middle fingers (Fig. 2), (2) combined orthodromic sensory and antidromic motor fibers by means of surface electrodes placed proximal to the wrist following supramaximal stimulation of the median nerve in the palm distal to the transverse carpal ligament (Fig. 2), and (3) combined orthodromic sensory and antidromic motor fibers by means of surface electrodes placed proximal to the elbow following supramaximal stimulation to the median nerve proximal to the wrist (Fig. 3). Surface recording was accomplished by means of plastic mounted electrodes one cm. in diameter having a distance of 2.5 cm. between centers. The electrodes were held in place by hand or with an elastic strap.

PLACEMENT OF ELECTRODES FOR EFFERENT CONDUCTION STUDIES OF THE MEDIAN NERVE

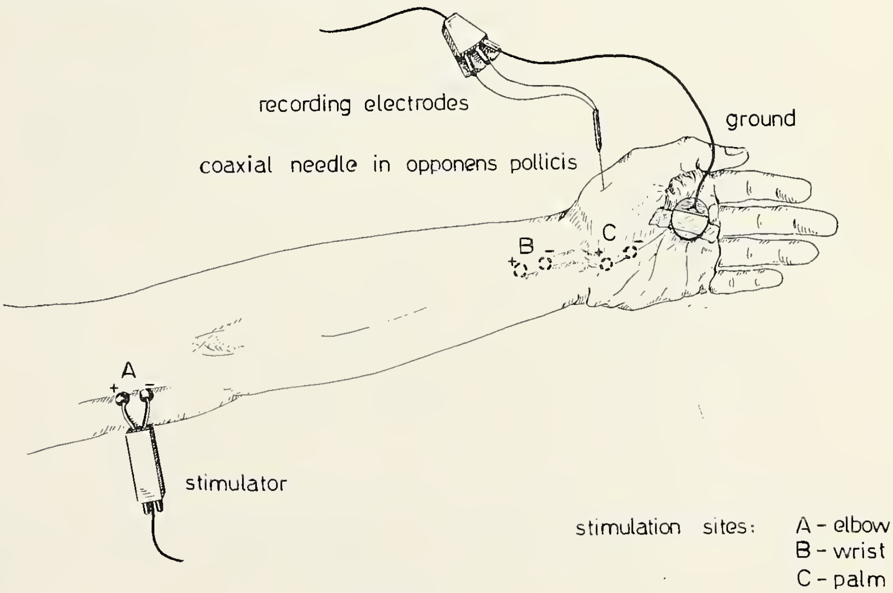

Figure 1

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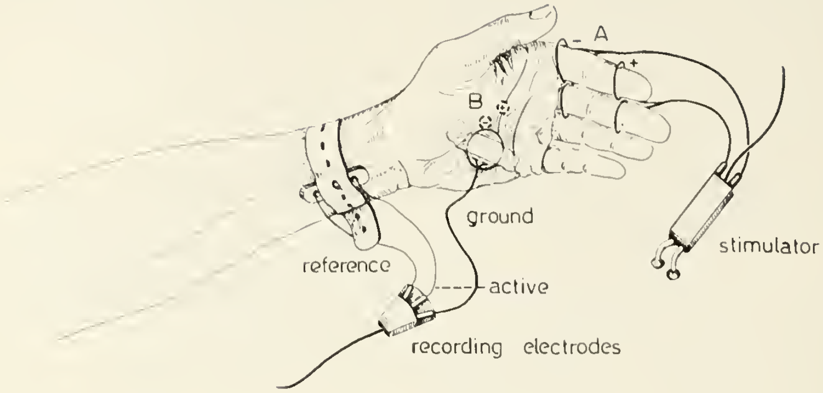
* TECA Model B and Model J.

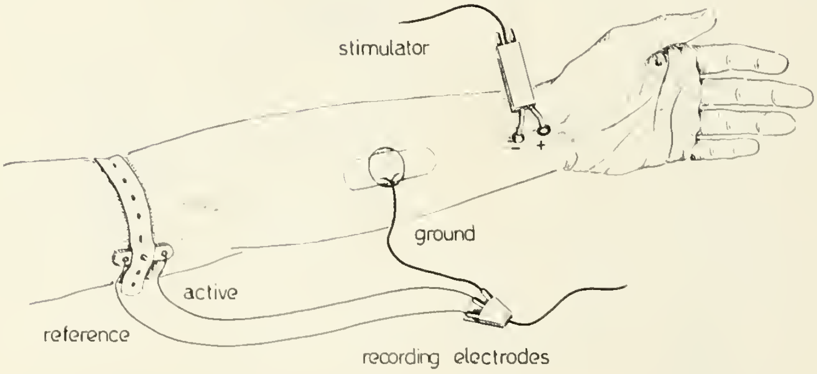
PLACEMENT OF ELECTRODES FOR AFFERENT CONDUCTION STUDIES OF THE MEDIAN NERVE



A - digits to wrist: orthodromic sensory technique
B - palm to wrist: orthodromic sensory, antidromic motor technique

Figure 2

PLACEMENT OF ELECTRODES FOR AFFERENT CONDUCTION STUDIES OF THE MEDIAN NERVE



wrist to elbow: orthodromic sensory, antidromic motor technique

Figure 3

Measurements of conduction latency were made to the initial deflection from the baseline of the evoked muscle potential and to the peak of the negative spike of the evoked nerve potential. The amplitude of the evoked nerve potential was recorded.

When appropriate the ulnar nerve was tested. The evoked afferent combined nerve potential from the orthodromic sensory and antidromic motor fibers was registered by means of surface electrodes placed proximal to the ulnar groove at the elbow. The ulnar nerve was stimulated supramaximally proximal to the wrist. If the response was of low amplitude (less than 25 microvolts or not recordable), the evoked efferent motor response was also tested. While recording from an appropriate muscle, the ulnar nerve was stimulated supramaximally (1) at the wrist, (2) distal and (3) proximal to the ulnar groove at the elbow. Conduction velocities were calculated for both forearm and ulnar groove.

A needle electromyogram (EMG) was obtained from the opponens pollicis and other muscles of the upper limb as judged appropriate from clinical signs.

Results of Electrical Examination

Electrodiagnostic testing for CTS was clearly positive in nineteen of twenty patients. Two patients with unilateral symptoms were diagnosed as bilateral CTS following electrical testing, changing the classification to eleven patients with unilateral and nine with bilateral CTS. Interestingly, one patient with bilateral symptoms had relatively more electrical abnormality on the less symptomatic side. One patient with bilateral CTS, a farmer, also demonstrated ulnar nerve-compression in the ulnar groove bilaterally.

Data from electrodiagnostic testing pre-operatively is shown in Table 1 and summarized in Table 2. Determinations critical to the diagnosis of CTS are (1) distal motor latency from wrist to opponens pollicis, (2) motor conduction velocity through the carpal tunnel, (3) distal sensory latency and amplitude from fingers to wrist, (4) latency and am-

TABLE 1

MEDIAN NERVE PREOPERATIVE RECORDINGS

				MOTOR						*SENSORY*				*COMBINED† CARPAL TUNNEL*				*COMBINED FOREARM*			
		Patient		*FV m/s*		*CTV m/s*		*DL ms*		*Lat. ms*		*Amp. uv*		*Lat. ms*		*Amp. uv*		*Lat. ms*		*Amp. uv*	
	#	*Sex*	*Age*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*
RIGHT	1	F	55	53	53	32	35	4.5	4.5	4.0	3.0	10	40	2.5	2.0	50	150				
	2	F	56	60	60	15	40	7.0	4.0	0.0	3.5	0	20	0.0	2.0	0	30	4.0		30	
	3	F	45	54	55	29	42	5.2	4.0	3.5	3.2	20	50	2.5	2.0	60	200				
	4	F	44	52	50	35	58	5.0	3.6	3.0	3.0	5	25	2.0	2.0	75	150				
	5	F	57	57	51	20	47	7.0	3.7	0.0	3.0	0	10	0.0	2.0	0	60	4.0		15	
	6	F	30	47	52	30	40	5.0	4.0	4.2	3.8	25	50	3.0	2.5	75	100				
	7	F	41	55	56	33	38	4.8	4.5	4.0	3.2	15	30	3.0	2.0	20	50				
LEFT	8*	F	30	61	61	44	44	4.5	4.2	3.0	2.8	50	40	2.0	1.8	150	175				
	9	F	37	53	60	38	21	4.5	6.0	3.0	0.0	10	0	2.0	2.0	30	10				
	10	M	19	59	66	46	0	2.9	4.1	2.5	3.6	45	10	1.5	2.2	150	25				
	11	F	57	52	52	33	19	4.5	6.0	3.0	3.0	20	5	2.0	2.0	50	20				
BILATERAL	12	F	53	44	44	20	17	6.5	7.0	0.0	0.0	0	0	0.0	0.0	0	0	5.0	4.8	15	15
	13	F	71	44	53	12	24	7.1	5.6	0.0	0.0	0	0	0.0	0.0	0	0	4.2	4.2	5	10
	14	M	56	54	54	17	27	8.7	7.0	0.0	0.0	0	0	0.0	2.0	0	5	4.5	4.5	10	15
	15	M	50	53	53	38	38	5.0	6.0	3.0	4.3	10	10	0.0	0.0	0	0	5.0	5.0	40	15
	16	F	74	52	57	14	20	7.0	5.5	0.0	0.0	0	0	0.0	0.0	0	0	4.5	4.5	20	10
	17	F	62	40	48	14	35	8.0	4.5	0.0	4.5	0	20	0.0	2.5	0	20	5.0	5.0	10	15
	18	F	39	46	51	14	54	8.0	4.0	0.0	4.0	0	10	0.0	0.0	0	0	4.0	4.0	15	15
	19	F	41	52	52	23	25	6.0	5.0	0.0	4.5	0	5	0.0	3.5	0	10	4.0	4.0	10	10
	20	F	50	45	56	28	20	4.5	5.5	3.7	4.5	20	15	2.5	0.0	10	0	4.0	4.0	20	20

* Electrodiagnostic studies are within normal limits. The clinical symptoms and signs included pain in the palm, positive Tinel sign at the wrist and sensory deficit over the middle finger. Sensory afferent response from stimulation of the middle finger alone yielded bilateral latencies of 2.8ms and amplitudes of 30uv on the right and 20uv on the left.

† Distances between cathode and distal recording electrode varied from 6.5 to 9.0 cm.

MOTOR represents efferent recording; SENSORY, COMBINED CARPAL TUNNEL, AND COMBINED FOREARM represent afferent recording.

TABLE 2

VALUES IN CARPAL TUNNEL SYNDROME MEANS AND VALUE LIMITS

Value†	*Eleven Unilateral Hands*		*Eighteen Bilateral Hands*	*Total Affected Hands*
	Unaff.	Aff.		
Forearm Velocity				
Mean (m/s)	54.7	56.1	49.9	52.3
No. less than 50 m/s	0	1	7	28%
Carpal Tunnel Velocity				
Mean (m/s)	41.9	27.8	24.4	25.6
No. less than 30 m/s or no response	0	6	14	69%
Distal Latency				
Mean (ms)	4.1	5.4	6.2	5.9
No. more than 4.5 ms	0	8	15	79%
Sensory Latency				
Mean (ms)	3.1	3.5	4.1	3.8
No. more than 3.8 ms or no response	0	7	16	79%
Sensory Amplitude*				
Mean (uv)	32	16	13	15
No. less than 10 uv	0	5	12	59%
Carpal Tunnel Latency				
Mean (ms)	2.0	2.4	2.6	2.5
No. more than 2.5 ms or no response	0	4	15	65%
Carpal Tunnel Amplitude*				
Mean (uv)	102	57	11	43
No. less than 30 uv	0	6	18	83%

† The means do not include instances in which the values were not recordable.

* In unilateral cases the affected hand showed values 50% or less than the unaffected hand for the sensory amplitude in 10 of 11 cases and for the carpal tunnel amplitude in 9 of 11 cases.

plitude from palm to wrist, and (5) bilateral comparison of these values. Registering an evoked afferent response from the median nerve from wrist to elbow was of value in localizing conduction disturbance to the carpal tunnel, if, for example, number 4 (above) were absent. The afferent response between wrist and elbow, however, can be affected by retrograde changes in the nerve or by a generalized peripheral neuropathy.

In all eleven normal hands distal latency (DL) did not exceed 4.5 milliseconds (ms) while in most of the twenty-nine affected hands it exceeded 4.5 ms. Carpal tunnel velocity (CTV) exceeded 30 meters per second (m/s) in the normal hand and was less than 30 m/s in most affected hands. Sensory latency (SL) was 3.8 ms or less in the normal hand and exceeded 3.8 ms or was not registered in most affected hands. Sensory amplitude was 10 microvolts (uv) or more in the normal hand and was less than 10 uv in most affected hands. Carpal tunnel latency (CTL) was 2.5 ms or less in the normal hand and exceeded 2.5 ms or was not registered in most affected hands. Carpal tunnel amplitude (CTA) was 30 uv or more in the normal hand and less in most affected hands. Sensory amplitude of the affected hand was 50% or less than that of the normal hand in ten of eleven unilateral cases. The CTA was similarly affected in seven of eleven unilateral cases. The forearm velocity averaged 55 m/s in unaffected and 52 m/s in affected hands. Carpal tunnel velocity averaged 42 m/s in unaffected hands and was reduced in comparison with forearm velocities. In affected hands CTV averaged 26 m/s. The nerve tended to be more severely affected in bilateral than in unilateral cases (table 1, 2).

Following initial evaluation surgical decompression was accomplished on twenty-two hands (seven bilateral, eight unilateral cases). All patients were improved and essentially free of symptoms following surgery. Five patients were selected for postoperative followup study from seven to twenty-three months following release. All patients demonstrated electrical evidence of improved conduction through the carpal tunnel. In three cases values returned to normal by all measurements and in two only minor electrical abnormalities persisted (table 3). The fact that other observers have failed to corroborate this[6,7] suggests that release may not have been complete, that the involved nerves had been permanently damaged, or that other pathology was the cause of the symptoms.

Discussion

Anatomy

In its passage from the forearm into the hand the median nerve courses through the carpal tunnel (Fig. 4).[8-10] At best it is a tight fit. In company with the long distal flexor tendons the median nerve lies snugly surrounded by a thin perineural sheath which merges with the flexor synovialis. The rigid canal is bounded by bone and a dense unyielding ligament. The bones of the carpus by configuration form a concave groove volarly called the carpal groove. Certain landmarks are readily palpated. Medially, the pisiform can be felt (wrist flexion facilitates this) at the level of the distal wrist flexion creases where it lies within the tendon of flexor carpi ulnaris. About one inch distal to the pisiform and slightly lateral to it can be palpated the deeply situated hook of the hamate. With firm pressure one can roll the superficial branch of the ulnar nerve over the hook. Laterally the tubercle of the scaphoid is an important landmark (each

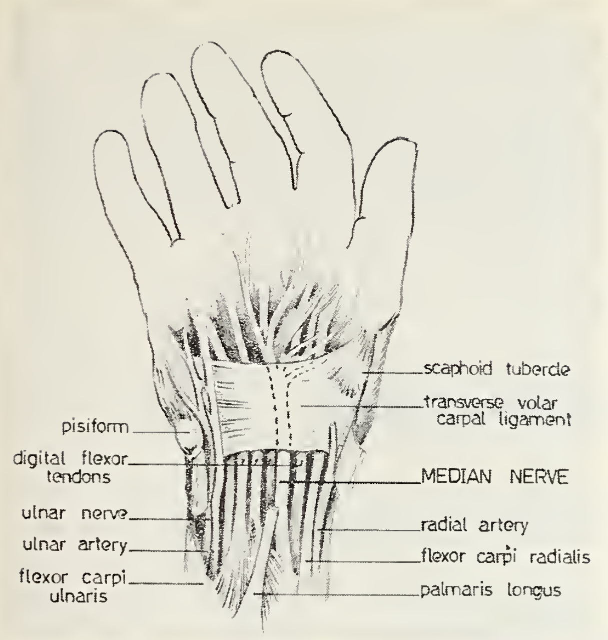


Figure 4

finger on flexion points to it).[11] It is palpable at the distal wrist flexion crease, slightly lateral to the tendon of flexor carpi radialis. Distal to this a forward projection of the trapezium is difficult to feel. The transverse volar carpal ligament attaches to these bony anchors. The ligament is composed histologically of dense collagen fibers. Flexion of the wrist forces the median nerve to arch over it. This fact is the anatomic basis for the wrist flexion test of Phalen.[12]

Normally the median nerve in the hand supplies palmar sensation to the lateral 3½ digits and the adjacent lateral palm. Importantly, the median nerve transmits most of the sympathetic nerve supply to the hand.[13] The motor branch of the median nerve, found at the level of the distal flexor retinaculum, supplies 2½ thumb intrinsic muscles (abductor pollicis brevis, opponens pollicis and the superficial head of flexor pollicis brevis).[8] An understanding of this basic anatomy is necessary for comprehensive diagnosis and treatment.

Diagnosis

In most cases of carpal tunnel syndrome the diagnosis can be suspected on the basis of history alone (Fig. 5). Women are more frequently affected than men. The right hand is more commonly involved. Symptoms are most common between ages thirty to sixty. Numbness and tingling are common symptoms.[12,14,15] Patients are usually unaware of the detailed anatomic distribution of these symptoms, and will report them in all digits, only to admit in retrospect the characteristic distribution. Pain is often experienced and, it should be emphasized, may be felt anywhere along the course of the median nerve and not only in the hand.[16] Pain in forearm, elbow, arm, shoulder and even neck may therefore obscure the diagnosis. Symptoms prominent in the middle finger, however, should especially alert one to the possibility of carpal tunnel syndrome.

Although symptoms may appear around the clock they characteristically awaken the patient during sleep, and she may volunteer that she gets up, walks about shaking and rubbing the affected hand to "restore the circulation". Specific manual activities or positions, especially if prolonged, may aggravate symptoms. As pressure and touch sensibility is obtunded the patient may experience clumsiness of

TABLE 3

MEDIAN NERVE EFFERENT AND AFFERENT RECORDINGS

(pre- and postoperative)

		MOTOR						*SENSORY*				*COMBINED CARPAL TUNNEL*				
		FV		*CTV*		*DL*		*Lat.*		*Amp.*		*Lat.*		*Amp.*		
	Patient	*m/s*		*m/s*		*ms*		*ms*		*uv*		*ms*		*uv*		
	Sex/Age	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	
RIGHT	F 57	57	51	20	47	7.0	3.7	0.0	3.0	0	10	0.0	2.0	0	60	Preop.
	7 mon.	57	56	40	47	4.0	3.7	3.0	3.0	5	20	2.0	2.0	25	40	Postop.
	F 30	47	52	30	40	5.0	4.0	4.2	3.8	25	50	3.0	2.5	75	100	Preop.
	23 mon.	49	53	40	50	4.2	3.7	3.0	3.0	25	50	2.0	2.0	100	100	Postop.
LEFT	F 57	52	52	33	19	4.5	6.0	3.0	3.0	20	5	2.0	2.0	50	20	Preop.
	11 mon.	54	52	38	38	4.5	4.0	3.0	3.0	15	25	2.0	2.0	60	100	Postop.
BILAT	F 41	52	52	23	25	6.0	5.0	0.0	4.5	0	5	0.0	3.5	0	10	Preop.
	19 mon.	53	54	40	50	4.2	4.2	0.0	3.3	0	15	2.2	2.0	25	50	Postop.
	F 50	45	56	28	20	4.5	5.5	3.7	4.5	20	15	2.5	0.0	10	0	Preop.
	10 mon.	56	56	39	35	3.8	4.0	3.0	3.5	50	30	2.0	2.3	125	100	Postop.

the hand, with difficulty performing refined tasks such as buttoning buttons, threading needles, and so on. Simultaneously complained of is the tendency to drop things (e.g. dishes, light utensils) and to knock things over. Because of the injured nerve contact with objects elicits inadequate tactile and proprioceptive sensory response.

Every examination for CTS must include observations for (1) Tinel's sign of formication,[17] (2) production or aggravation of symptoms on wrist flexion (Phalen),[12] and (3) atrophy and weakness of thenar muscles (Fig. 6). Tinel's sign is positive when light percussion over the median nerve at the wrist flexion crease produces tingling which extends into

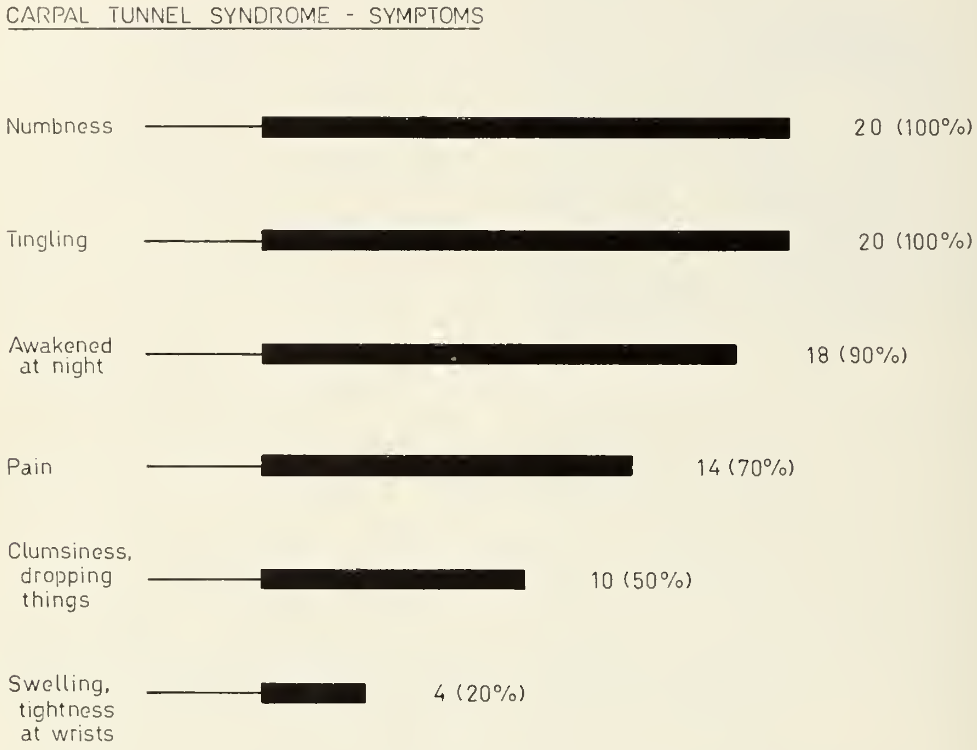


Figure 5

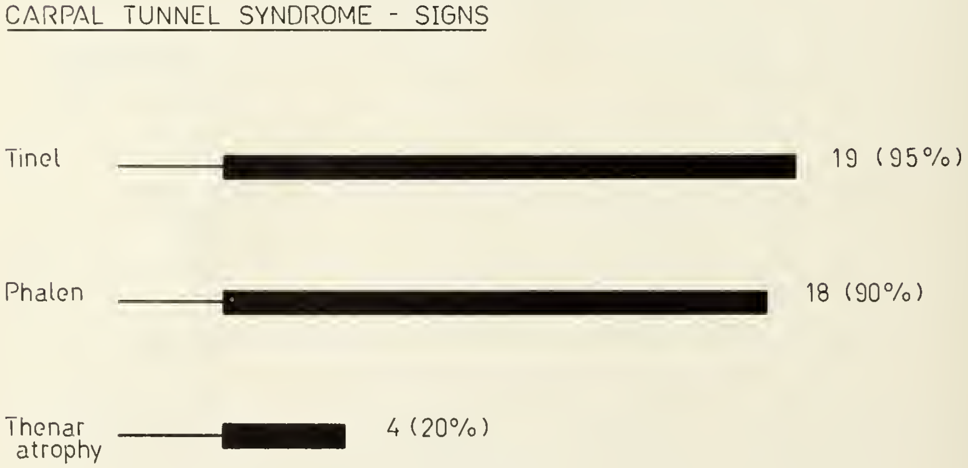


Figure 6

one or more digits. Tinel in 1915 used the word "fourmillement", best translated as "crawling of ants". The wrist flexion test of Phalen is positive when numbness and paresthesia in the median nerve distribution in the hand are reproduced or exaggerated by full wrist flexion for thirty to sixty seconds. Because the position of extreme wrist flexion compresses the median nerve the Cotton-Loder position (maximal wrist flexion and ulnar deviation), still used by some physicians in the treatment of Colles fractures, must be condemned.[13] Inspection of thenar muscles for atrophy and testing for weakness are best accomplished while the thumb is being resisted in a position of abduction and opposition.

Electrodiagnostic testing is of localizing value to show that median nerve function only *distal* to the wrist is abnormal.[11,18,19] Occasionally, in more severe cases, retrograde changes affect conduction in the nerve proximal to the wrist. Since electrical testing is the most objective means for establishing the diagnosis of CTS it is indicated in all clinically suspected cases. For example, recording from the opponents pollicis with a coaxial needle electrode permits stimulation of the motor nerve in the palm for direct calculation of motor conduction velocity through the carpal tunnel. Recording the afferent nerve potential at the wrist following stimulation in the palm adds another measurement of median nerve conduction through the carpal tunnel. Bilateral comparison of amplitudes of the sensory and the carpal tunnel nerve potentials in unilateral cases can assist measurably in making the diagnosis when clinical examination is equivocal.

Differential diagnosis involves several considerations.[9,12,14,20] Cervical disc pathology (herniation, degeneration, spondylosis and the like) is commonly confused with carpal tunnel syndrome. Every now and again one encounters a patient with CTS who has failed to enjoy improvement after surgery for "cervical disc disease". Small wonder. Adequate workup should include evaluation of cervical spine and chest to rule out pathology in these areas. Cervical rib, Pancoast tumors (at the apex of the thorax, involving the contiguous brachial plexus), acromioclavicular and shoulder joint problems (bursitis, rotator cuff lesions, bicipital groove syndrome), elbow lesions (including lateral epicondylitis) as well as problems at the wrist such as DeQuervain's tenosynovitis, all must be considered. The arthritides including gout must always be excluded.[21]

It should be emphasized that although most cases of CTS are probably best classed as idiopathic, some reflect generalized disease. In such cases appropriate therapy should be directed toward the underlying disease. CTS is due either to increased volume of the structure within the carpal tunnel or to diminished size of the tunnel itself. Acromegaly, amyloidosis, diabetes, gout, hemangiomata, menopause, myxedema, osteoarthritis, pregnancy, rheumatoid arthritis and tumefactions are but some of the many reported associated conditions. During surgical release a diagnostic biopsy may confirm one of these diagnoses.

Treatment

Meticulous surgical division of the entire transverse volar carpal ligament under direct vision offers the best chance for prompt and lasting relief. With few exceptions CTS reflects a mechanical problem and therefore is best treated mechanically.[20] Occasionally other methods of treatment may be effective.[12] When sleeping with the wrist flexed is a cause of symptoms, the use of a neutral position night splint is sometimes helpful. When inflammatory change in synovium, paratenon or associated structures is responsible for symptoms the careful injection of an appropriate steroid around but not into the median nerve may provide relief of symptoms.

All of the releases in this series were done under general anesthesia. The technique is as follows: A pneumatic tourniquet is placed at the level of midhumerus. The extremity is held elevated for several seconds and wrapped snugly with an Esmarch bandage to help empty the vascular tree. The pneumatic tourniquet is inflated to appropriate pressure and the Esmarch bandage is removed. A gently curving incision is made just to the ulnar side of the thenar eminence flexion crease and carried proximally as far as the distal wrist flexion crease (Fig. 7). (This incision can be extended as indicated proximally to allow a volar synovectomy if necessary.) The incision is carried through subcutaneous areolar and fatty tissue to the transverse carpal ligament. This ligament is most safely incised under direct vision to avoid injury to the important motor branch to the thenar musculature. Normally this branch arises from the radial side of the nerve. Rarely it may arise from the ulnar side of the nerve.[22] It usually is found within a separate "tunnel" through the transverse volar carpal ligament.[23] An accessory branch piercing the retinaculum and arising proximally has been described by Linburg and Albright.[24] The importance of following all motor

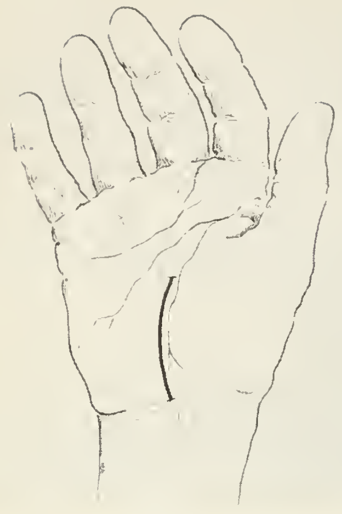


Figure 7
Incision for carpal tunnel release.

fibers to the thenar musculature after division of the transverse volar carpal ligament cannot be overemphasized. Once the distal ligament has been transected its proximal portion is easily and safely divided with small partly-opened scissors, using a gentle pushing motion. At this point the pneumatic tourniquet is released and loosened on the arm to prevent venous occlusion. Firm pressure on the wound with saline-moistened sponges is maintained for five minutes, the wound then gently irrigated and any remaining bleeders clamped and ligated. Only when hemostasis is adequate is the skin closed. The sutures are tied only tightly enough to hold the skin edges in gentle approximation. Often no dressing is necessary but, if used, bandaging should not be for compression, and should never be a substitute for adequate hemostasis. It is important that postoperative management not contribute to prolongation of disability. Therefore, not only is bandaging purposefully kept at a minimum, but also early activities are encouraged. Consequently patients in this series who have undergone simultaneous bilateral releases have been able to maintain their own self-care. Patients are usually discharged from the hospital the day following surgery. They are advised to elevate the operated hand as much as possible for the first several days. Gentle washing is permitted. Active finger flexion and extension exercises are started immediately. Skin sutures are removed at about ten to twelve days. Gradual resumption of unrestricted activity follows within three to six weeks.

Summary

Nerve conduction study is a precise means for diagnosing CTS. Expanded techniques are described here for compiling more information about nerve conduction through the carpal tunnel. Patients with symptoms of discomfort in the hand or upper limb should be considered for electrodiagnostic testing. Particularly in patients with confusing symptomatology this approach facilitates appropriately directed treatment. Careful release as described performed prior to permanent damage to the nerve should result in lasting symptomatic and objective improvement.

Acknowledgement

The authors with to express thanks to Pat Becker for the illustrations, graphs and typing of this manuscript.

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Judges For The Connecticut Physicians' Art Association

April 25, 26, 27 1972

The three member panel to select winning entries in the 1972 Art Exhibit has been announced by Dr. Eugene Rightmyer, President and Mrs. Orvan Hess, Vice President.

Mrs. Ethel Stauffer, Hamden, painter and teacher, past president of the New Haven Paint and Clay Club, member of the Connecticut Academy of Fine Arts and the Pennsylvania Academy of Fine Arts; Gail W. Martin, Hartford, Professor of Art at the University of Hartford, member of the Connecticut Water Color Society and the Connecticut Academy of Fine Arts; Mrs. Jean Day Zallinger, North Haven, illustrator, painter and teacher at the Paier School of Art in Hamden.

Connecticut Medicine

Editorials

World Heart Month: April 1972

The world health day which is celebrated each year April 7, the anniversary of the coming into force of the constitution of WHO, will be in 1972 the "Day of the Heart." "Your heart is your health" is the WHO theme. This day will also mark the beginning of the World Health Month which is being organized by the International Society of Cardiology, The International Federation and WHO. The main theme chosen for World Heart Month is "Through Research to Prevention" although other slogans may be used in different countries according to local custom and language. The theme symbolizes the urgent need for community prevention programs based on solid scientific evidence.

The purpose of the "Month" is to demonstrate the world over that the scourge of cardiovascular disease is common to almost all peoples although it may be particularly "burning" in certain areas. Everyone must be aware that in general these diseases are the first cause of death among adults in many countries before cancer, accidents, tuberculosis or others. As an example is chronic heart disease which has reached epidemic proportions particularly in industrial countries striking more and more at younger subjects. Premature death in man's productive years thus represents a truly irreversible brain drain which no country can afford. The developing countries and the tropical regions of the world are similarly affected by hypertension, cardiomyopathies due to rheumatic fever and Chagas' disease, to mention only two.

Public awareness, education and motivation in other words, active participation is the first aim of the Month. The second is to stimulate all health workers to prepare a frontal attack against the growing challenge and to promote further action aimed at preventing and controlling cardiovascular diseases and eliminating their etiologies and pathogenesis where these are not clarified. In addition, active participation and cooperation between health workers and the general public means mutual assistance in creating a favorable milieu for research investigations, prevention studies, screening, as well as raising funds for a concerted effort at both the national and international level.

It is obvious that the final solution of the complex and baffling problems of heart disease must come from the laboratory and the scientist. Scientific and medical problems cannot be solved by meetings but rather by new ingenious observations and investigations. A great step toward a solution, however, comes from recognizing the important questions and even phrasing them correctly.

It has also become increasingly clear that the first line of defense in medical care is to have an informed patient and his family. If the individual does not understand what he must do to preserve his health, if he cannot recognize when he needs help and if he is not prepared to take personal responsibility for his health, to take the appropriate steps to obtain this help then much of the world's present medical knowledge will find no practical application. Materials both audio-visual and printed are being prepared by WHO and other agencies and will be supplied in time for use in the press, radio, television and other media. But the responsibility for preparing and carrying out national campaigns remains the duty of national organizations. Only they know the best targets and the ways and means for achieving them in different cultures and taking into account the local differing features of cardiovascular disease.

All should feel concerned: the physician advising his patient; the doctor lecturing in his community; the medical educator teaching his student; the scientist explaining the purpose of his work. All should feel committed. Heart disease is not just a degenerative disorder or an appendage of old age against which little or nothing can be done. It is the epidemic of this century. Its ravages can at least be checked or reduced if not entirely eliminated. We started late to think about what society should do to prevent pollution and preserve a healthy environ-

dvertisement

> *"The history of science, and in particular the history of medicine . . . is . . . the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."*
>
> *—George Sarton, from "The History of Medicine Versus the History of Art"*

Should nongovernment scientists and physicians play a role in drug regulation?

Opinion

Results of a questionnaire to 7000 physicians:

82.8%
Physicians should play a role

78.3%
Independent scientists should play a role

69.8%
Medical academicians should play a role

Should nongovernment scientists and physicians play a role in drug regulation?

Doctor of Medicine

Herbert L. Ley, Jr.,
M.D., M.P.H., Formerly
Commissioner, F.D.A.
(1968-1969)
Currently Medical Consultant

In order for drug regulation to be effective, participation in the regulatory process from nongovernment physicians and scientists must be encouraged. Without such involvement, there will continue to be a high degree of controversy surrounding any regulations promulgated by the Food and Drug Administration.

There are two areas in which participation and communication by nongovernment physicians and scientists could significantly improve the process of regulation. First, scientists and physicians throughout the country could become involved in consulting relationships with the Food and Drug Administration in important scientific areas while regulatory policies are being evolved. If nongovernment professionals could bring their expertise and experience to bear early in the decision-making process, they would have less reason to criticize the final outcome.

Secondly, practicing physicians, academic physicians, and academic-based scientists could make it their business to comment on proposed regulations appearing in the Federal Register. Ideally, a system could be instituted whereby medical, scientific and technical people could see the Federal Register regularly, and provide the Food and Drug Administration with a body of opinion that has so far gone unheard. The FDA is caught among pressures from industry, Congress, the Presidential Administration and consumers. It should also feel pressures from practicing physicians and scientists.

In order to become more involved in these stages of the drug regulatory process, nongovernment physicians and scientists should begin to exercise their influence through their respective professional organizations, state and national medical societies, and specialty groups. Logically, a letter from these organizations representing a collective opinion has far greater weight in the regulatory process than individual letters. If the Food and Drug Administration receives opinions from these organizations early, before a regulation gets into the Federal Register, they are in a good position to respond with further study and review. Without such dissenting opinions, there is very little incentive to make changes in proposed regulations.

One instance in which practitioners did influence drug regulatory affairs in this way is the recent controversy that arose over the legitimacy of drug combinations. The strong opinion of practitioners on the value of such medication in clinical practice played a very prominent role in making the Food and Drug Administration modify its rather restrictive policy.

Another way in which practitioners can effectively influence drug regulations is by working with drug manufacturers conducting clinical trials of chemotherapeutic agents. When a drug is rated other than effective it may only mean that there is a lack of controlled clinical evidence as to efficacy. Thus, physicians might offer to conduct clinical studies that could help keep a truly effective drug in the marketplace. The treatment of diseases such as diabetes and angina are areas where the practitioner can aid in clinical studies because patients suffering from these diseases are rarely found in the conventional hospital setting.

By working with ethically and scientifically sound study designs in his everyday practice, the practitioner could begin to play an important part in determining official ratings on drug efficacy.

Nongovernment physicians and scientists and the FDA should also improve their lines of communication to the public. The medical community must develop a voice every bit as loud as that of the consumerists, the press, and others who sometimes criticize without complete information. If not, much of what the medical community *and* federal regulators do will often be represented in simplistic and somewhat misleading terms.

One illustration of the misuse of the media in this regard is the recall of anticoagulant drugs several years ago. This FDA action was given publicity by the press and television that went far beyond its probable importance. The result was a very uncomfortable situation for the practitioner who had patients taking these medications. Since the practitioner and pharmacist had not been informed of the action by the time it was publicized, in most states they were deluged with calls from worried patients.

The practitioner can attempt to solve these problems of inadequate communication in several ways. One would be the creation of a communications line in state pharmacy societies. When drug regulation news is to be announced, the society could immediately distribute a message to every pharmacist in the state. The pharmacist, in turn, could notify the physicians in his local community so that he and the physician could be prepared to answer inquiries from patients. Another approach would be to use professional publications the practitioner receives.

All of this leads back to my opening contention: if drug regulation is to be effective, timely, and related to the realities of clinical practice, a better method of communication and feedback must be developed between the nongovernmental medical and scientific communities and the regulatory agency.

dvertisement

One of a series

ue

Maker of Medicine

Henry W. Gadsden,
hairman & Chief Executive
Officer, Merck & Co., Inc.

In my opinion, it is the esponsibility of all physiians and medical scientists o take whatever steps they hink are desirable in a lawnd regulation-making rocess that can have fareaching impact on the ractice of medicine. Yet many events in the recent ast indicate that this is ot happening. For example, it is apparent from rug efficacy studies that he NAS/NRC panels gave ittle consideration to the vidence that could have een provided by practicng physicians.

There are several current levelopments that should ncrease the concern of racticing physicians about rug regulatory affairs. One s the proliferation of malractice claims and litigation. Another is the effort by government to establish the relative efficacy of drugs. This implies that if a physician prescribes a drug other than the "established" drug of choice, he may be accused of practicing something less than first-class medicine. It would come perilously close to federal direction of how medicine should be practiced.

In order to minimize this kind of arbitrary federal action, a way must be found to give practitioners both voice and representation in government affairs. Government must be caused to recognize the essentiality of seeking their views. One of the difficulties today, however, is that there is no way for concerned practitioners to participate in the early stages of decision-making processes. They usually don't hear about regulations until a proposal appears in the Federal Register, if then. By that time a lot of concrete has been poured, and a lot of boots are in the concrete.

Physicians in private practice, and particularly clinicians, should press for representation on the advisory committees of the Food and Drug Administration, joining with academic and teaching hospital physicians and scientists who are already serving. Though practitioners may not have access to all available information, the value of their clinical experience should be recognized. Clinicians, for example, rightly remind us that difficulty in *proving* precise effects does not necessarily mean a drug is ineffective.

Unless practitioners are more involved in drug regulations, it will be increasingly difficult for the pharmaceutical industry and scientists elsewhere to make optimal progress in drug development. The benefit/risk ratio must be re-emphasized, and as part of this it must be acknowledged that benefit can come from the judgments of medical science as a whole. Even this concept, unfortunately, is not always accepted in drug regulatory processes. For example, if current medical opinion holds that an excess of total lipids and cholesterol in the blood is probably predisposing to atherosclerosis, and if a drug is discovered which reduces total lipids and cholesterol, the drug ought to be accepted *prima facie* as a contribution to medical science . . . until someone disproves the theory. The sponsor should not have to prove the theory as well as to develop and test the drug.

I feel a major new effort must also be made to erase the feeling of mistrust of medicine and of medicines that seems to be growing in the public consciousness. Triggered primarily by strident announcements in Washington, people are reading and hearing confidence-shaking things almost continuously. Although challenge and awareness are essential to medical advancement, our long-term goal is constructively to build, not destroy. This means strengthening patient-physician relationships based on mutual confidence and trust. And in matters of health policy, it means working toward participatory rather than adversary proceedings—where everyone with an interest and a capacity to contribute has an opportunity to be heard . . . and, if that opportunity is not spontaneously afforded him, he may seek it.

Opinion & Dialogue

What is your opinion, doctor?
We would welcome your comments.

P·M·A

The Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W., Washington, D.C. 20005

ment. Let us not make the same mistake in preparing the attack against heart disease.

The young adult and future generations are at stake. Diseases of the heart and blood vessels are no more strictly a medical and scientific domain. They have become a social problem with serious human and economic implications. World Heart Month in April, 1972, should be the beginning of constant and persistent future widespread activities. Let each and all of us become involved. The life you help save may be your own.—L.H.N.

Theory And Practice

We generally practice medicine that we think we know but 10 years later we often find we really didn't know some of it. Some of this arises from apriori grounds which suggest that the remedy should be effective. In the past much treatment was given on theoretical grounds which we now recognize as having been useless or harmful. Familiar examples are bleeding, starving, purging and prolonged bed rest for all manner of maladies. Today there is wide agreement that treatment should be given because there is evidence that it is effective and not because on theoretical grounds it should be effective.[1]

This doctrine that treatment should depend on practice not theory alone has not yet been universally accepted, as witness many regimens of diet prescribed and many physiological therapies which are often given for theoretical reasons. One example is our changing attitudes towards treatment of patients with myocardial infarction by bed rest. Originally it was said that an infarct does not become replaced by firm fibrous tissue until 6-12 weeks after onset and, therefore, it was held that the patient must rest for a long period. Before 1939-45 similar reasoning condemned post-operative patients to prolonged spells of bed rest.

Treatment of myocardial infarction changed when it was recognized that in the sitting position the heart does less work than when the patient is lying in bed. Getting a patient out of bed after surgery early was found to reduce convalescence and prevent pulmonary embolism. What these developments meant was that the correct means of obtaining evidence about the value of a treatment is to study a controlled series of alternate patients being kept in bed for a specific period and alternate patients being allowed up when they feel so inclined.

The important source of such errors is our misunderstanding as to what constitutes evidence. A clearer grasp of this problem is to recognize when a proposed practice is a hypothesis based on theoretical knowledge or a conclusion following definite evidence that it works in practice. It may seem self-evident that the value of a remedy can only be assessed from observations on the progress of the whole patient. Instead certain physiological changes may be used as the sole criterion. Thirty years ago shocked patients who were hypothermic were treated with warm blankets and when the temperature was restored to normal we congratulated ourselves because we had given such obvious benefit, but the patient died.

A few years ago the subjects of cardiogenic shock were given such pressor agents as noradrenaline. Their blood pressures which were previously unrecordable rose strikingly to the satisfaction of all concerned except of the patient who died. A recent article on the treatment of shock recommends laying the patient flat or if the central venous pressure is low, elevating the foot of the bed, O_2 in high concentration and a simple dose of 1 mg metaraminol tartrate intravenously in cardiogenic shock. Then rapid use of plasma or plasma substitutes followed by blood, electrolyte solution or plasma when the C.V.P. is normal or reduced.

Sodium bicarbonate is suggested in severe acidosis continuous infusion of isoproteronol for patients with cardiogenic shock or with hypovolemic shock in whom transfusion has elevated the C.V.P. without restoring cardiac output. Also recommended is alpha-adrenergic blocking agent phenoxybenzamine when there is extreme peripheral vasoconstriction but cardiac filling is adequate. Other familiar examples of treatment given because it causes physiological effects are lidocaine after cardiac infarction to prevent ventricular ectopic beats and intravenous lactate or bicarbonate to correct the acidosis of diabetic ketosis.

Shock is a complex condition with many causes and an infinitely variable natural history. The only way of determining whether any particular remedy saves the lives of shocked patients, and life or death as the only criteria needed, is to study a controlled series, one patient being given and the next denied the remedy. The object of giving lidocaine after myocardial infarction is or should be to save life. At present it is assumed but not proven that because it prevents ventricular ectopic beats it will prevent ventricular fibrillation. In the case of diabetes ketosis insulin itself will abolish the acidosis of diabetic ketosis. Thus far no one has found that lactate or bicarbonate will save more lives than insulin alone.

In many situations in addition to those mentioned above, evidence as to the value of remedies is lacking. When some one is advocating a remedy it is clearly necessary to distinguish between hypothesis and conclusion, theory and practice. If there is evidence that a remedy is beneficent it should be made known. If no evidence exists then the proposed remedy is based on theory.[2]

Such a distinction between theory and practice is always made in this journal which requests of contributors to correct manuscripts which do not make such a distinction.—L.H.N.

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Three Decades Of Progress In Liver Disease

In the past three decades there has been a remarkable upswing of interest in liver disease as well as in all other branches of biomedical science. Much of this has been due to increase in available diagnostic methods which have been developed. We have now biochemical tests which help us to understand functional and structural alterations in hepatic parenchyma, its circulation and the biliary tree. Needle biopsy, cholangiographic techniques, angiographic techniques and scintiscanning have all grown up in these years. The last utilizes I.V. injection of either colloidal or soluble radioactive molecules to demonstrate space occupying lesions within the liver, structural and functional abnormalities of the hepatic parenchyma, reticuloendothelium and vasculature and to a lesser extent patency of the biliary tract. Despite these advances, not all need for precise diagnostic methods have yet been met as illustrated by problems found by viral and drug induced hepatitis.[1]

There has also been marked progress in therapy of liver disease. More effective measures for the control of ascites, hemorrhage, shock and intercurrent infection. There has grown knowledge concerning recognition and importance of correcting nutritional deficiencies and abnormalities of electrolytes and water balance. In addition, new methods have been devised for treatment of those complications more specifically related to liver disease such as bleeding from esophageal varices and hepatic coma. These measures are nonspecific and are not aimed at the repair of the underlying hepatic lesions, nevertheless, they may contribute to recovery or prolongation of survival by preventing further liver damage or by reducing the mortality of life threatening complications. These procedures have definitely increased the life span of patients with Laennec's cirrhosis over the past 3 decades.

Current therapeutic methods, however, are still deficient in many respects, particularly in the management of esophageal hemorrhage, hepatic coma and the hepatorenal syndrome. It is true that portacaval shunting usually prevents recurrence of esophageal bleeding but it not infrequently results in chronic hepatic encephalopathy. Patients with Laennec's cirrhosis who have experienced esophageal bleeding continue to have a poor prognosis. However, measures aimed at improving the blood ammonia levels do prove effective in the control of chronic hepatic encephalopathy attributable to surgical spontaneous portacaval shunting or to the type of acute hepatic coma provoked by G.I. bleeding, excessive protein intake or undesirable diuretic therapy

Such measures almost always fail, however, when coma is due to severe hepatocellular failure secondary to advanced cirrhosis or massive hepatic necrosis. It is apparent, therefore, that accumulation of blood ammonia is not the only metabolic abnormality involved and that the development of more effective therapy for hepatic coma must await further clarification of its pathogenesis. The efficacy of exchange transfusions in the treatment of massive hepatic necrosis with coma is still in doubt. However, some patients show remarkable rapid clearing of the sensorium although transient, and this suggests there we must look carefully in such individuals for additional clues to the pathogenesis of hepatic coma.

The hepatorenal syndrome is another serious complication of liver disease for which as yet no effective therapy is available. Apparently the kidneys themselves are not involved since they function normally when transplanted. If the pathogenesis of this disturbance can be elucidated probably effective therapy will be found. Unfortunately, the syndrome appears almost exclusively in patients with advanced and frequently irreversible hepatocellular failure, so that the correction of the renal defect per se could prove fruitless.

Few therapeutic measures have been developed to correct or modify lesions that affect the liver. Phlebotomy has proved effective in recovering excess tissue iron in patients with hemochromatosis. In some, it appears to improve hepatic function and prevent tissue progression. Penicillamine frequently relieves the neurological manifestations of Wilson's disease by elimination of excess tissue copper. Whether or not it prevents the progression of the accompanying hepatic lesions is not established.

Klatskin has produced histologic evidence to indicate that corticosteriods and azathioprine suppress hepatic parenchymal necrosis and inflammation in some patients with acute and chronic inflammatory disease of the liver. This is often accompanied by improvement in hepatic function and remission of symptoms. What is still uncertain is whether such therapy shortens the duration of or prevents progression in this heterogenous groups of diseases.

Considering the substantial progress made in the past three decades, the accelerated pace and widened scope of current research efforts as well as the availability of new investigative techniques, there is every prospect that answers to most of the unresolved problems in liver disease will be found in the foreseeable future.—L.H.N.

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Oral Contraceptives And Thromboembolic Disease

The question of whether or not there is a relationship between the use of oral contraceptives and the occurrence of thromboembolic disease has been studied by both retrospective and prospective methods. In retrospective studies there appeared to be an association between oral contraceptives and thromboembolic disease. In prospective studies no such relationship has been fund. Drill[1] considers the various reasons for this discrepancy and also reports the results of prospective studies in which no relation was found between oral contraceptives and thromboembolic disease.

In prospective studies the drug is administered to groups of women and the occurrence of thromboembolic disease is recorded. Based on this direct measurement, the incidence of disease for 1,000 women per year can then be calculated and compared with the normal incidence of thromboembolic disease. Thus prospective studies provide for a direct evaluation of disease incidence and conclusions related to the presence or absence of a cause and effect relationship can be made.

The data from 15 large scale prospective studies and from 53 small scale prospective studies published between 1963 and 1970 demonstrate that the incidence of superficial and deep-vein thromboembolic disease in women with and without predisposing causes is not increased when oral contraceptives are employed. This conclusion is based on the result of over 80,000 women receiving oral contraceptives for more than 1 million cycles or 81,778 women years of drug use. The average normal incidence of superficial and deep-vein thromboembolic disease in women of childbearing age is 2.3 cases per 1,000 women per year. This incidence seems not to increase during pregnancy when estrogen secretion is increased or when oral contraceptives are empolyed. Drill found the incidence of thromboembolic disease in the users of oral contraceptives to be 0.97 cases per 1,000 women per year. Similarly, Guttmacher and Perkin[2] found an incidence of thromboembolic disease based on 26,884 women years to be 0.63 cases per 1,000 per year.

Retrospective studies on the other hand differ fundamentally from prospective studies. The retrospective case control studies on oral contraceptives do not measure the normal incidence of thromboembolic disease. Instead, they compare the frequency of the use of oral contraceptives between a group of patients with thromboembolic disease and one without. Thus a retrospective study can only provide a hypothesis that an association exists. As Professor Mainland, author of Elementary Medical Statistics states, a second retrospective study does not

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add weight to the first retrospective study as it provides again only the same hypothesis.

When one considers the result of prospective studies, many bits of information fall into place which were confusing in the past. For example, the high output of hormones, particularly estrogen during pregnancy is not associated with an increased incidence of superficial and deep-vein thromboembolic disease. We should also expect a high proportion of cases within the first few months of drug administration. This point was examined in the retrospective studies as patients admitted to hospitals in Great Britain or the U.S.[3] with the finding that such association does not exist.

Also there is no dose response relationship between oral contraceptives and thromboembolic disease. Doses as high as 100-120 mg per day have been administered without any adverse effect.[4] If the use of oral contarceptives is related to the occurrence of thromboembolic disease then patients with such a history should be sensitive to these drugs. The findings are, however, that such women do not experience an increase in thromboembolic disease when oral contraceptives are employed. Finally, women who develop thromboembolic disease respond to the usual therapeutic measures while continuing to take oral contraceptives. Obviously, if oral contraceptives were a causitive factor, it may be expected that the disease would not resolve in the face of continued treatment. No such difficulty is apparent in the several case reports presently available.

It is clear that the present data are medically consistent. Prospective studies demonstrate that oral contraceptives do not increase the incidence of venous thromboembolism of the lower extremities. It would seem that the hypothesis of increased risk in the use of contraceptives from retrospective studies must therefore be abandoned.—L.H.N.

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The Doomsday Syndrome

There are some who believe and insist that science and technology will soon bring society to its knees even though for the best part of a century before, it was supposed that social progress must rest on technical progress of some kind or another. In fact, people took the view that there would be no limit to the advancements of the human spiral so long as people could be liberated from the need for drudgery so as to keep alive and from the restraints of the environment in which they found themselves and which was almost by definition hostile. It is hard to imagine a more complete contrast than that between the way in which technical developments used to engender optimism and the way in which the prospect of technical innovation has now become a kind of a threat.

Several arguments have been used in recent times to highlight the sense of impending disaster. The world's population is for example one of the most common and, of course, it is well known that the population of the world cannot continue to grow at the present pace for decade after decade. The prospect of unregulated population growth has apparently caused great consternation in the past few years. Some have held quite openly that what they call the "population bomb" must spell disaster for society at large not merely for those unfortunate communities where the pace of growth is the greatest. And what kind of disaster? The world will run out of food. The mid-seventies will be the time when famine is rife, when tens of millions of people will die each year of starvation. It seems almost an indecent question to task whether disaster is as near as all this talk suggests.

In the first place the population of the world has grown less quickly than its production of food. The Food and Agricultural Organization of the UN, in its time one of the most fervent beaters of the calamity drum, has statistics which show that the production of food per head of population has actually increased by 5 percent between the late 30's and late 60's. At present, many developing countries are found more with the prospect not of famine but of problems of marketing harvests of cereals. Now they need commercial machinery, long familiar in the agriculture of nations in which subsistence agriculture has long since disappeared.

Whatever the prophets of doom may say, it does seem that famine will not be the most obvious cause of calamity in the next decade. Even though the doomsday view on this point is inappropriate, this does not imply that the pace of growth of the world's population brings no unfortunate or unforeseen consequences or that nothing needs to be done about it.

When looked at in historical perspective one is impressed with the way in which it seems to have taken the human race from the beginning of its evolution, 2 million years, up to the beginning of the 19th Century to reach one billion, another century to add a second billion and merely half a century since then to double the population of the world. On the face of things this is much more than exponential growth. Yet there are reasons for thinking that the growth of a human population is much more complicated and subtle than the growth of a population of bacteria in a Petri dish.

In Britain, the medieval population was held in check by a succession of infectious diseases from plague to influenza. Even though the agricultural revolution in the 18th century increased the productivity—the population growth did not keep pace with it. It looked as if it is quite possible for a growing population to limit its rate of growth even without the full apparatus of modern contraceptive techniques.

The rapid growth of the world's population in the past 30 years is almost directly attributable to the way in which better medicine and better insecticides (used against the mosquito which carry malaria, for example,) have enabled hard pressed communities to keep their children alive until middle age. Many people begot many children because infant mortality was high and they wanted at least one male to grow up. If we can reduce infant mortality there develops a falling birth rate as is now apparent in places such as Hong Kong and Singapore.[1] What this implies is that there is every reason to expect that social forces will in due course help to control the population in developing countries as it has in Britain. To be sure it is important that steps should be taken to encourage this development. If we wish to bring about a stable solution we need to advocate those kinds of social innovations that might encourage stability than to complain that famine is just around the corner. When a nation becomes economically prosperous this is the precondition for population stability.

The alarm which attends public discussion of the population problem crops up everywhere. For example pollution is now so widely held to be a threat to the survival of orderly society that there is danger of distortion of a sense of social priorities. DDT and other chlorinated hydrocarbons are good examples. They are persistent, toxic to animals which concentrate them. In very large doses they may increase the incidence of tumors in mice. The persistence of DDT argues for close control of the way it is used. However, an over zealous scorn for DDT and related chemicals should not be allowed to rob the world of the large benefits they may have in the prevention of malaria, in the improvement of precisely the kinds of agricultural productivity that has been one of the problems of how to feed the growing populations and which are in any case a good deal less damaging to the environment than some of the other materials, sodium arsenate, for example, which they replace.

To be sure, it is always possible to hope that more subtle methods of controlling insect populations ranging from the deliberate infection with parasites to the use of pheromones for baiting insect traps may in due course help to control populations of unwanted insect pests without causing serious side effects. But those who advocate abolition of DDT on the grounds that it will bring calamity should realize that biological control is still a technique applicable only in particular circumstances.

Population and pollution are only two of the spectres which perplex commentators on the relationship of science and technology with society. Some feel that CO_2 in the atmosphere will eventually produce such a powerful greenhouse effect that the antarctic ice cap wil be melted although nobody can be sure that the effect will be that predicted. There are certainly many people who seem anxious in the long run to demonstrate that the world is about to end.

The real threat of global catastrophe posed by nuclear weapons especially, is a part of the explanation where there should be so much concern about global calamity that might arise. This threat of nuclear war on a catastrophic scale is now in retreat. That the 50's should have left behind such a sense of bewilderment about the way to strike a balance between the useful application of technology and the unwanted side effects which it can produce is a special phenomenon of great interest. We need a doctor of society to help steer us into the right path.[2]—L.H.N.

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Depression: The Commonest Disease

Many doctors treat depression, the "commonest disease", every day either the obvious ones that come straight out and declare themselves or the less obvious ones masked in a wide variety of disguises. Not the transient mood or appropriate reaction to grief, but depressive illness noted for its chronicity and the depletion of energy which results. It is an insidious disease which often creeps up gradualy and is unnecessarily disabling. As it affects mostly the productive 35+ age group, the hazard extends to all the patient's associates.

In spite of its being such a common condition depression is often missed. The physical symptoms, depressed mental and physiological function, may come first to the attention of the physician, respond poorly to conventional treatment and much time may be wasted before the true diagnosis is made, during which the patient's total vitality is lowered. The simple depression shows first and foremost sadness and dejection, helplessness and self-reproach. There occurs a general loss of interest in all the good things of life; loss of appetite, loss of sexual drive, loss of pleasure in spite of hobbies, reading or work. Increased boredom and lassitude sets in, crying spells, anxiety attacks and morbid brooding. The guilty self-reproach may go to the point of suicidal thoughts.

Mental functioning is impaired. The patient can't concentrate or make decisions. His memory is unreliable. He may slip into neurotic or behaviorial or psychotic reactions or disguises. Especially may there arise fatigue, headache, all kinds of gastrointestinal disturbances, bowel dysfunction, cessation of menstruation and impotence may develop. The cardiovascular system seems to become upset especially if it is old or damaged. Muscles are tired, disturbances of the sleep pattern occur in the form of early morning waking or conversely oversleeping. Many fruitless investigations and many needless operations are done on patients when their real problem is depression. It seems as though feeling bad and guilty and wanting punishment, he hopes for some unpleasant investigation or treatment to pay himself off.

The family doctor is in a much stronger position than the specialist in diagnosing depression since he knows his patient, the family, how they express their need for help. A valuable clue in detecting depression is a previous emotional illness either in the patient or his family. There may be a family pattern of mood swings. The physician will know the loss of a job or a lover, crippling debts or other crippling activities which might lead him to expect a depressive reaction in the patient. We must always remember that the loss of vitality is a symptom of an actual or imagined loss of something valued in the patient's life.

Anyone who has lost something is going to feel badly about it but after a reasonable period of time a continuing reaction to loss is a "reactive depression" a neurotic illness in which the process within the patient is mostly psychological. At the other end of the scale, of course, are the depressions which seem mostly constitutional, an inherited predisposition not readily related to environment or if it is, so out of proportion as to be bizarre.

We must remember that some depressive illness seems to be related to something physical happening in the body either a natural happening such as the process of involution, senescence or disease such as pernicious anemia, nutritional deficiencies, parasitic infestations, endocrine disorders, myxedema, diabetes and hypoparathyroidism. Many infections can leave a person depressed, particularly virus infections, influenza and many others. Exhaustion is a potent force in promoting depression. Exhausting work or play or exhausting grind for an examination or writing against a deadline also may lead into depression.

It is nice to make a satisfactory physical diagnosis. Then one can offer some definitive treatment. It is necessary to look deeply into the patient's physical complaints to catch the lurking physical disease. Sometimes a psychosomatic depressive equivalent will turn up but the physical diseases are relatively few while depression is a very common illness. Therefore, the physical and psychological should go along together. The patient must always be seen as a whole individual not as a collection of parts. However, it is very satisfying to see a depressed patient and detect the previously undiagnosed myxedema or diabetes, treat it and vanquish the depression.

To make a diagnosis of depression on positive grounds, you have to piece together a reasonably complete picture from symptoms, history and dynamics. The classic situation in depression is one of actual or imagined loss. What has the patient lost? Losses can be very obvious or very subtle. If his wife died six months ago and the mourning period is protracted, it is easy to see a "pathological grief reaction." If her daughter got married and moved away the loss is a little more subtle and neurotic. If he lost his job this may affect the whole family with hardship yet the main threat may also be loss of prestige. Retirement after years of hard work may be a bitter blow when it comes because of the loss of function and purpose. The loss may be one of belief or ethic although the patient may have lost her religious values or his honor or he may no longer believe in the goals toward which he was striving.

So the situation is one of loss, and of consequent sadness. In between comes anger. When something is taken away from you the first reaction is to be angry. As long as anger can be effectively challenged in action you don't get sad. With a cause to fight for, something practical can be done. In this situation reaction to loss is less likely to be depressing. Behavior equivalents of depression involve a channeling outward of their anger. Everyone knows the value of hard work to dispel grief. If, however, the anger in response to a loss is inexpressible because there is no one to express it to or because you are at fault and can't reasonably complain about, say, losing your job or because the loss is too subtle to be understood, then there is no place for the anger to go but in. Inturned anger is destructive to the individual although in a particular sort of way we still intend to get back at the outside person who has let us down.

There is another feeling besides anger that depressed people have. They lack self-esteem, have self-depreciation, feel guilty. The patient with depression is really suffering, the anguish, the pain, must never be underestimated nor must the risk of self-destruction. Depressive illness in the "raw" or in its many disguises can be recognized by the alert physician. At the stage when the disease first becomes evident the patient is usually physicaly intact. Unlike many of the great killers, depression when recognized early is curable. Potentially, then, there is greater satisfaction in treating depression than in treating cancer or heart disease or strokes.

All physicians should be aware of the high incidence of depression not only among their patients but also among themselves. Its masks are many and its costs are high in depletion of energy morbidity and even mortality. It is illuminating that religions and cultures where guilt is less stressed, the individuals suffer less from depression.—L.H.N.

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Science Tools: Impendance Phlebography

Thromboembolism is generally considered to be one of the most common causes of death after immobilization for any cause. With the use of radioactive fibrinogen it has been possible to demonstrate that 30 percent of all patients over the age of 40 develop clots in the deep leg veins. The striking thing is that most of such patients show no clinical evidence of this disease. Some recover spontaneously. However, even a patient who is totally asymptomatic and apparently healthy may succumb suddenly with an unsuspected pulmonary embolus. Furthermore, even those asymptomatic patients with occult thrombosis may years later develop significant morbidity from the postphlebitic syndrome.

We need a non-invasive method to detect deep vein thrombosis which can be readily and repeatedly performed. One such procedure developed by Wheeler and his colleagues is based on the observation that during inspiration there occurs fluctuations in leg venous blood volume. The normal changes in venous hemodynamics that accompany respiration are significantly altered in the presence of thrombophlebitis. The presence or absence of fluctuations can be recorded by an instrument which measures the electrical impedance of the limb.

The instrument consists of a battery operated four electrode impedance measuring system. The current used—less than one milliampere is imperceptable to the patient and cannot stimulate the heart. It is applied to the calf via circumferential electrodes. Voltage fluctuations in the electrical field are measured through a second pair of electrodes connected to a Kelvin bridge current. First the bridge is balanced with an internal resistance equal to that of the patient and then voltage changes can be read directly from a volt meter or observed on a stip chart recorded. The recorder is so calibrated that a 10 mm. deflection of the stylus equals 0.1 percentage change in the patient's resting baseline impedance.

The patient is placed in the supine position with chest and legs at the same level. The foot is placed in slight external rotation so that the weight of the lower leg is borne more on the lateral aspect of the leg than on the calf muscle. The knee is then flexed about 20 degrees to diminish slightly impedance excursions from pressure on the popliteal vein. The examiner now asks the patient to take a deep breath with his diaphragm and abdominal muscles. The patient must be relaxed, breathing with his diaphragm, his leg muscles must be relaxed and not tense since this will introduce artifacts in the tracing. The patient now inhales slowly for 2-3 seconds holds his breath for 5 seconds and then exhales slowly. After several tries consistent impedance tracings are obtained.

Wheeler and his group performed 3,000 examinations on 760 patients mostly males. Eighty-one were undergoing elective abdominal surgery and 47 open heart surgery. Some studies were performed on patients considered vulnerable to deep vein thrombosis because of chronic immobilization due to spinal cord injury (32 patients or diminished peripheral arterial blood flow (110 patients).

Their results are striking. Sixteen of 32 patients with paralyzed lower extremities showed deep vein obstruction. In those with severe cardiac disease undergoing open heart surgery 19 of 43 had abnormal preoperative phlebograms and half of the normal ones became abnormal post-operatively. Of 43 patients suspected of having pulmonary embolism 27 (63 percent) demonstrated deep vein obstruction. If, however, pulmonary embolism was documented by lung scan and pulmonary angiograms, then 16 of the 18 showed deep vein obstruction. Two patients who were believed to have pulmonary embolism but did not have it also had normal phlebograms. Finally, of the 81 patients undergoing elective abdominal surgery, 22 (27 percent) had abnormal postoperative impedance phlebograms.

The chief limitation of impedance phlebography is the necessity of the patient to take a deep breath. If he is unresponsive, critically ill or in great pain it may be impossible to obtain an adequate respiratory excursion even if the deep veins are fully patent. In actual practice, however, impedance phlebography has proved applicable to at least 95 percent of the patients in Wheeler's study. They even succeeded in getting good excursions in unconscious patients with spontaneous respirations or with assisted breathing.

The method is simple accurate and should prove a boon to detecting a common complication which is treatable but often goes unrecognized at present.—L.H.N.

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A Coming Era Of Antiviral Chemotherapy

The results of research during the last 10 years herald a coming era of antiviral chemotherapy. We have learned the basic steps of viral replication in host cells out of which have come the efforts to prevent viral infection. In the first step, the virus adheres to the host cell, then enters it. There its nucleic acid is uncoated. Now the virus nucleic acid must make copies of itself and the viral proteins. In general, viruses containing DNA core first code for RNA (translation) which attaches to ribosomes to synthesize the proteins of the virus. These proteins include enzymes necessary to make copies of DNA virus (replication) and proteins which are put together with the viral DNA to form mature virions (assembly).[1]

The RNA core viruses may serve directly as messenger RNA or can be transcribed to a complimentary RNA. Again the RNA of the virus must be replicated, the viral proteins synthesized must assemble with the replicated RNA to form the mature virion. The RNA core mammalian tumor viruses are exceptional in that virion RNA first codes for DNA replication. The biochemical events occurring during the replication cycle of these viruses are as yet unknown. Finally, mature viruses must be released from the infected cell to continue the infection. Thus, the major approaches to viral chemotherapy depend on first interference with the entry of the virus into host cells, or second on inhibition of replication of the viral nucleic acid genome, or third on inhibition of synthesis of the viral proteins.

Inhibition of viral entry has been reported to be successful with amantadine which causes a selective dose related inhibition of influenza B2 infection in tissue culture and in mice. The action is not virucidal but instead prevents virus penetration of host cells very much like a high antibodytiter. Recently, it has been shown in human volunteers that if the substance is given 24 hours before inoculation it can prevent infection in an exposed person.

Inhibition of replication of the viral nucleic acid genome is now also possible by compounds that inhibit the enzymes synthesizing nucleic acid precursors. One of these is 5-iodo-2' deoxyuridine (IUDR) which depletes the pool of thymidine triphosphate necessary for DNA synthesis. IUDR inhibits the growth of vaccinia and herpes simplex viruses in vitro and is effective in herpetic keratitis in rabbits and man and has been used successfully in herpetic encephalitis.

Cytosoine arabinoside also acts against core DNA viruses. It has been used successfully in disseminated Herpes Zoster and severe progressive varicella Zoster. It is, however, not an ideal agent because it prevents the synthesis of host cell DNA.[2] Three other substances under study to prevent viral intra cellular synthesis are rifampicin against tumor virus; bezemidole (HBB) against type II polio virus and others. Finally is tripanoside ethidium bromide which is a potent inhibitor of DNA synthesis of the leukemia virus and others but it is too toxic for use in man.

Then there are the chemical substances which inhibit the synthesis of viral proteins. Once such is thiosemicarbazone which is used to prevent clinical smallpox in contacts with smallpox patients.[3] It is effective in the prodromal stage but not after the skin lesions have appeared. There are also untoward side effects but may indeed be a broad spectrum antiviral agent.

Rifampicin is an antimicrobial agent of low toxicity used in treatment of tuberculosis and menigococcal carriers. However, it also inhibits replication of adenovirus and blocks the formation of proteins for vaccinia virus. It has an effect against Shope fibroma virus. Recently, Israeli investigators discovered that rifampicin is also effective against trachoma inclusion conjunctivitis (TRIC).[4] They also showed that rifampicin inhibited the formation of lesions resulting from the infection. However, in such cases, it has to be locally applied in cream or ointment. Much may be expected from this in the future.

Much has been written about interferon stimulators in the treatment of viral infections.[5] This endogenously produced protein seems to interfere with the viral messenger RNA from combining with cellular ribosomes. As a result, viral proteins are not synthesized. At present interferon stimulators that are clinically useful are not available.

It can be seen that agents affecting specific viral processes during each step of replication have been discovered. However, many obstacles remain to be overcome in search for clinically effective antivirals. We need suitable test systems for screening antiviral agents for use in human diseases. Such tests should be rapid, inexpensive and should reveal not only the antiviral effects but also the toxicity of the test substance. Furthermore, the tests should be sensitive and should require only small quantities of the test substance. Tissue culture has now become the primary test method although here too there are numerous problems to overcome.

Obviously, toxicity must be very low to justify chemotherapy of most self-limited viral diseases. Moreover measurements of drug efficacy in self-limited diseases are difficult to obtain and hard to interpret. In using chemotherapy against viral epidemics the value of such prophylaxis must be weighed against the possible loss of build-up immunity in the population.

Clearly, much more investigations of structure-activity relationships will be necessary to define the kinds of chemical structures which are useful especially because of need for low toxicity in man.

Despite all these obstacles, the future of antiviral chemotherapy is at present very bright indeed.—L.H.N.

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On Digoxin, Hexachlorophene, Saccharin And The FDA

At least three events have recently occurred to focus on the behavior of the FDA. One deals with digoxin, one with hexachlorophene and one with saccharin. In the case of digoxin, a clinical report from Columbia College of Physicians found that of 4 lots of tablets of digoxin chemically equal were biologically not equal for when administered to nominal volunteers the serum levels were found to vary markedly. In one instance, the serum level was seven times that obtained from other products. The clinicians recommended that evidence of biologic equivalency of digoxin products should be required in addition to chemical equivalence.[1]

The FDA response was to assert that biologic equivalence in drugs is too knotty a problem for immediate official action. Another response was to report that chemical analyses have shown that some batches of digoxin varied from 60 to 200 percent of the declared amount of the active ingredient. Biologic equivalence is an important pharmacologic principle and certainly digitalis preparations would be a good place to start applying it. For this is a drug with a proper therapeutic level which is narrow and is balanced between a practically ineffective level when too low or a toxic effect when too high. The FDA, however, has neglected to require that potent drugs like digitalis be manufactured in reliable form.

The misadventure with regard to hexachlorophene is another of FDA "regulatory nightmare" on its hasty, precipitate ban on this valuable agent for bathing the newborn. For here is a product, pHisoHex (Winthrop), about as well established in the health care field as shoes are in our clothing customs. Save for the tragic consequence growing out of the restriction, the whole matter could be characterized as just another regulatory misadventure, which against the record of oral contraceptive scares, combination ingredients ban, and once the labeling of a tennis shoe as a drug,[2] should astonish nobody at all. The point is that if the findings are preliminary and obviously inconclusive, one should wait for more conclusive evidence before acting. Staphylococcal outbreaks were occurring in hospital nurseries where the use of HCP had been discontinued and the FDA had to backtrack. There is a lesson here. The FDA's action was at most a monumental goof and at best a poorly managed action of the bureaucracy.

With the bitter taste left by the cyclamate farce still in its mouth the FDA must have received with some trepidation the news that a study in Wisconsin has come up with tentative evidence of bladder tumors in rats fed on a diet heavy with saccharin. This time the FDA's response was to take saccharin off the list of food additives generally recognized as safe (GRAS) and to take action on an 18 months old recommendation of the National Academy of Sciences (NAS) by suggesting that the average daily intake of the sweetener should be limited to 1 gram per person (about 60 tablets or 7, 12 ounce bottles of so-called diet drinks.[3] Fortunately, barely a ripple of public anxiety was touched off and thankfully it was not followed by the precipitate worldwide reaction that greeted the tentative findings in 1969 that cyclamates produced bladder cancer in rats fed huge quantities over a period of 2 years.[4]

The tentative findings on saccharin were made in the laboratory of the Wisconsin Alumni Research Foundation (WARF) through a study supported by the Sugar Research Foundation. No details of the experiments have been released but it is understood that the tumors were found in 3 out of 20 rats fed a diet of 5 percent saccharin during a 2 year feeding experiment. The experiment has not yet run its full course and the suspected tumors have still to be examined by pathologists for signs of malignancy. However, the WARF experiment is only one of about 12 2-year feeding experiments being conducted and the FDA says none of the other experiments have so far produced any adverse reactions.

This is a case in which nobody can accuse the FDA of precipitate action in its handling of saccharin. In fact, quite the reverse. It waited from July, 1970, when the committee of the NAS recommended that saccharin be taken off the GRAS list almost a year until June 25, 1971, before taking action on the committee's suggestion. Such a delay would be difficult to justify by most criteria. However, it allowed the dust to settle over the cyclamate ban and perhaps forestalled a panic reaction to tentative results.

The possibility that saccharin may cause bladder cancer in rats fed massive doses of the sweetener also adds a final note of irony to the farce that surrounded the removal of cyclamate from the market in 1969. We might recall that the key experiment that led to the ban consisted of feeding rats not pure cyclamate but a mixture of cyclamate and saccharin in a 10:1 proportion. The FDA then assumed it was the cyclamate that caused the cancer not the saccharin or a reaction between the two. The finding now that saccharin is suspected of causing identical bladder tumors is ironic to say the least.—L.H.N.

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The Emergency Coronary Care Ambulance: Theory And Practice

Some 300,000 men and women die each year during the terrible minutes or hours between an acute coronary attack and their arrival at the hospital. Studies on survival of patients both in hospital and outside who were certified as dying of coronary artery disease or arteriosclerotic heart disease showed that the median time of death lay between 3 hours and 30 minutes after the onset of the attack for men and 6 hours, 18 minutes for women.[1] This observation laid greater stress on the speed in the provision of acute coronary care.

McNeilly similarly found that 60 percent of all deaths occurred outside the hospital. This also indicates that the problem of cardiac resuscitation in coronary artery disease is to a considerable extent an extra-hospital one. One would, therefore, suppose that among these there might be a special scope for the cardiac ambulance providing that medical aid is sought and the ambulance summoned without delay. If ambulances are staffed and equipped to stabilize the heart and prevent fatal arrhythmias would there be a substantial improvement in outcome?

Accordingly, Smyllie made a prospective study of patients with proved or likely acute myocardial infarction in Doncaster to determine the duration of the stages leading to admission to a coronary care unit (CCU) and to measure the survival time from onset of the attack in fatal cases either in hospital or outside and reported to the coroner. Out of it he hoped we could obtain some guidance about the possible impact of a coronary ambulance on mortality in Doncaster. Patients were drawn from two sources: admissions in one year to the hospital CCU from ten selected practices utilizing a "no refusal" service and second, all cases in the same year as diagnosed as coronary occlusion at necropsy by the coroner's pathologist.

Despite attempts to speed up admission of cases, the median time of admission was 3 hours and 22 minutes after the onset of the attack. The greatest delay was due to the patients, half of whom waited almost 2 hours or more before requesting medical assistance. This delay was minimal in 15 percent who notified within 15 minutes and maximal in 18 percent who waited 8 hours or more. In contrast, the ambulance service moved with gratifying speed collecting 95 percent within 30 minutes to the hospital. Delay in transferring from the accident and emergency departments to the CCU emerges as a factor of equal importance to one ambulance journey.

Smyllie examined the history of 51 total cases that were admitted to the hospital and 148 coroner's cases during the same period of 12 months. The median time of death were very different in the two series. 16.8 hours for the coroner's cases and 89 hours for patients admitted to the hospital. It is assumed that the rationale for coronary ambulance would be to provide coronary care for those patients who may die before admission to a hospital, that is those fatal cases at present referred to the coroner. Clearly death had occurred in 79 percent of coroner's cases before half of the hospital patients had requested medical aid. The provision of a coronary ambulance service to be called by the physician would result in advancing CC by a fraction of the patients' delivery time (12 minutes) at a point where the survival course is almost horizontal.

The speed of admission to the CCU after acute myocardial infarction in Doncaster compares quite favorably with experiences elsewhere in Britain. The sensitivity of the median times of preadmission stages to those found in Edinburgh and quoted by Gambier[2] reflects Smyllie's experiences also. Death after the onset of myocardial infarction is usually swift. The fact that the median delay in calling for help by the patient is 6 hours and 50 minutes, highlights one of the major obstacles preventing the coronary ambulance from reaching those patients who die soon after the onset of the attack and are referred to the coroner.

Appreciation of this fact that delay can be due to referral through the physician has led to an attempt to bypass primary medical care in acute myocardial infarction in the Belfast coronary care scheme where the family can call the ambulance. Apparently the delay operates in most places anyway. It seems clear from Smyllie's results that the provision of a mobile CCU to be alerted by the physician cannot be expected to contribute much to the saving of life with acute myocardial infarction especially in an area such as Doncaster where ambulance delay is minimal and certainly in areas where ambulance delays are not minimal.

In theory, of course, mobile emergency services should improve mortality. In one practice, obviously they did not. We await further experience to resolve this discrepancy between theory and practice.—L.H.N.

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McNeilly, R. H. and Pemberton, J.: Duration of last attack in 998 fatal cases of coronary artery disease and its relation to possible cardiac resuscitation. Brit. Med. Jr., 3:139, 1968.

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Muscular Platelets

(*Nature*, 234-252, December 30, 1971). An actin-like protein which may well prove to be completely identical with muscle action has been found in considerable amounts in nerve cells. Here it may be responsible for the mobility of the growing tips of axons.

Now Adelstein, Pollard and Kuehl have isolated a myosin-like as well as an actin-like protein from human blood platelets. Platelets in wound healing cause a retraction of clots and clearly such a function must depend on some sort of molecular contractile aparatus.

The myosin-like protein from platelets has a molecular weight of about 200,000, the same as that of rabbit skeletal muscle myosin. They also isolated another protein from platelets with a molecular weight of skeletal muscle actin 46,000.

It is reasonable to conclude that the molecular basis of contraction in platelets as in axons is in all essentials similar to that of skeletal muscle.—L.H.N.

Ethanol Produces Muscle Damage In Human Volunteers

(*Science* 175:327, 1972, Song, S. K. and Rubin, E.) Three human volunteers received repeated administration of ethanol (42 percent of total calories for 28 days). They developed increased serum creatine phosphokinase activity and also showed ultrastructural changes in skeletal muscle.

Since the heart is also a muscle, the data suggests the alcoholic cardiomyopathy results from ethanol toxicity rather than from nutritional or other factors.—L.H.N.

Marine Pollution

(*Nature*, 235:122, January 21, 1972) The Ocean Affairs Board of the National Research Council has put forward a plan for urgent studies to be made of materials, particularly heavy metals and radionuclides and their impact on the marine environment.

Emphasizing the fact that concern about the environment is not matched by adequate research and information gathering, the board recommends five chief areas of study: identification and routes of harmful materials, dispersal, biological and geochemical transfer effects on man and other life organisms and sites of final deposition.—L.H.N.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

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Summary of Actions
Council Meeting
Wednesday, March 22, 1972

I. Attendance

Present in addition to the Chairman, Dr. K. F. Brandon, and the Vice-Chairman, Dr. D. A. Grendon, were: Drs. Weber, Cramer, Spitz, Backhus, Granoff, Dean, Fabro, Hess, Bradley, Rem, Johnson, Ragland, Jr., Harwood, Pelz, Wilson, Roch, Nemoitin, VanSyckle, Friedberg, Harkins, Root, Jr., Freedman, Sprecace, Dambeck and Klare.

Also present were: Mrs. Lindquist, Dr. West (NHCMA), Mr. Olson (FCMA), Mr. Tomat, Mr. Sullivan and Dr. Richards.

Absent were: Drs. Nolan, Gardner, Palomba, Luby, and LaBella.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of February 17, 1972.

Date of Next Meeting

By prior decision of the Chairman, the next meeting of the Council had been scheduled for Wednesday, April 5, 1972.

III. Old, New and Special Business

Resignations, Appointments, Etc.

(a) *Chairman, Committee on Accident Prevention*: It was VOTED to accept with regret, and thanks for past service, notice that Isao Hirata, Jr., New Haven, will be unable to continue service on this Committee beyond the end of his current term (April, 1972). It was further VOTED to delete Dr. Hirata's name from the report of the Nominating Committee to be acted upon by the House of Delegates in April and to nominate Edward A. Rem, New Canaan, as chairman of the Committee for 1972-73.

(b) *Member, Committee on Allied Medical Services*: It was VOTED to accept with regret, and thanks for past service, the resignation of E. Tremain Bradley, Norwalk, as a member of this Committee, and to delete Dr. Bradley's name from the slate of nominees for the Committee to be transmitted to the House of Delegates for election in April.

Report—Committee on Medical Economics and Insurance

It was VOTED to receive for filing a report submitted by the Committee concerning proposed changes in the Society-sponsored "Major Medical Plan," and to approve the recommendations of the Committee that such changes be authorized for implementation by the Plan's administrator. In brief, the changes will be: (a) *Basic Plan* ($500 deductible) —increase in maximum benefits for a single illness from $10,000 to $15,000; increase in allowance for per diem charge for hospital care from $30 to $50, and, if in intensive care unit, $75 per day for up to 10 days. (b) *Modified Plan* (Blue Cross as deductible)—increase in maximum benefits from $10,000 to a range of $12,500 to $17,500 (depending on type of Blue Cross plan and amounts of benefits). (c) *Medicare Supplement Plan* (new)—$5,000 coverage (per benefit period per person) will be available to members enrolled in the Basic and Modified Plans upon reaching age 65 years, such benefits to be used for any purpose desired by the policyholder (such as private duty nurses, added costs of private room, etc.) as a supplement to Medicare benefits.

Report—Committee on Statewide Medical Planning

It was VOTED to receive for filing a report of this Committee concerning a study of the private practice of medicine; to approve, in principle, a proposal contained in the report for making such a study under the auspices of the Society; and to transmit the report and proposal to the House of Delegates in April with Council recommendation that it be approved, in principle, by the House. In brief, the study would include the office of the private practitioner as well as area group clinics, HMO's, etc.; the study would be financed by a grant of $250-300 thousand to the Society from HEW; personnel to conduct the study would be selected and employed by the Society, using grant funds; the materials and techniques used in making the study would be those approved by the Society, developed by three representative panels of physicians (CSMS members); and would require the voluntary participation in the study of approximately 200 physicians engaged in primary patient care (100 in the Greater Hartford area and 100 in the Greater New Haven area.)

Reports—Committee on Public Health

(a) *Re Routine Smallpox Vaccination*: The Committee reiterated its previous recommendation that the Council go on record as accepting the recent action of the State Public Health Council which advocates discontinuance of the routine vaccination of school children against smallpox, and to limit such vaccination international travelers, etc. who may be going to areas infested with smallpox. A motion to approve the recommendation of the Committee was lost. Thereupon, the Council VOTED to adopt the following motion:

> "That the Council of the Connecticut State Medical Society recognize the recommendation of public health authorities that routine smallpox vaccination of school children be discontinued, but express concern whether such discontinuance could lead to a resurgence of smallpox in the United States in the future."

It was further VOTED to transmit copies of this action to the State Commissioner of Health and to the president of the CSMS Section on Pediatrics.

(b) *Re Venereal Disease Education*: It was VOTED to approve a recommendation of the Committee that, in recognition of the growing problem of venereal disease in the state and the presently inadequate education of young people on this subject, the Advisory Committee on Physicians and Schools, in consultation with Norton G. Chaucer, Hartford, and George N. Bowers, Jr., Hartford, seek to reinforce health and sex education in the school system and to organize a program on sex education, stressing the subject of venereal disease where applicable.

It was further VOTED to recommend to the Committee on Public Health and/or the Advisory Committee on Schools and Physicians that consultation on this project also be made with Oliver L. Stringfield, Stamford, who has been doing outstanding work in developing an educational program on venereal disease for the students and faculties of the secondary schools in his area of the state.

In conjunction with the latter action, it was further VOTED to arrange for suitable recognition of Dr. Stringfield's work in this field to be made by the House of Delegates at its annual meeting in April via the awarding of a certificate for service.

CRMP

Communication — Chairman, CRMP Advisory Board: The Council VOTED to receive for filing a letter from Mr. Russell G. D'Oench, Jr., newly-elected Chairman of the CRMP Advisory Board, which reviewed some of the past differences between the Society and CRMP, particularly regarding the "full-time chiefs of service" program; expressed his "respect for the right and duty of the Society to vigorously contest any action of CRMP with which it may disagree"; and concluded with the hope "that the months ahead will generate new ways for us to work together for even better patient care."

It was further VOTED to respond to Mr. D'Oench's letter along the following lines: Thank him for his response to the question posed by the CSMS House of Delegates re increased costs to patients of the "3rd Faculty Program"; advise him that the Council will await with interest receipt of a promised further response to that question which will furnish the facts that CRMP expects to develop in the near future; reassure him that the Council and/or House of Delegates will continue advocacy of the Society's points of view which he indicates it is the "right and responsibility" of CSMS to do when such points of view differ from those of CRMP on matters pertaining to the delivery and financing of patient care in Connecticut; and that the Council shares his hope that future CSMS-CRMP relationships will be mutually cooperative and productive.

Report—Committee on PRO's, Foundations and HMO's

It was VOTED to receive for filing a report of the Committee which related the sense of discussions that have been held with representatives of the Connecticut Hospital Association concerning the possibility of forming a joint CSMS-CHA peer review-utilization review committee which might qualify for recognition by HEW if the pending Professional Services Review Organization legislation (Bennett Amendment) should be passed by Congress. It was further VOTED to authorize the Committee to continue to explore this possibility with CHA, using the following as guidelines:

Utilization Review is defined as the mechanism whereby the hospital medical staff assures itself and others that all health services provided are necessary, appropriate and of high quality.

The primary authority and responsibility for utilization review activities should be vested in the individual hospital medical staff.

An appeal mechanism should be defined which enables a third party purchaser of care, physician or patient to appeal a decision of a hospital utilization review committee.

A statewide utilization review panel, consisting of physicians, hospital administrators and others, sponsored by CSMS & CHA shall be created to act as an appeal board to resolve disputed decisions of local hospital utilization review committees. The decisions of the statewide utilization review panel shall be final and binding on the parties involved.

Third parties are encouraged to endorse the CSMS-CHA utilization review mechanism as the single, acceptable system for utilization review in Connecticut.

Informational Report—Changes in Regulations re Obstetrical Bed Utilization

It was VOTED to receive for filing, and as information, a report that the Public Health Council has amended the regulations governing the use of obstetrical beds for the use and treatment of patients other than obstetrical patients. In brief, the new regulations permit surgeons who are not obs-gyn specialists but who have gynecological privileges to admit clean gyn cases to obstetrical beds (formerly limited to obs-gyn specialists) and provide for the inclusion of one such surgeon on the advisory committee to the chief of a participating hospital's obs-gyn service (formerly limited to obs-gyn staff members).

Informational Article—"Can AHA Seize the Throne from AMA?"

Without vote, reprints of this article (Medical World News, 2/25/72) were received as information. In brief, the article describes the expanding interest of hospitals and their representative organizations, from the American Hospital Association down, in restructuring the American health care system with hospitals as the central core. The point is made that as hospital staff membership and privileges become of increasing importance to the practicing physician, membership in organized medicine could become of decreasing importance; i.e., the AHA could "seize the throne" of medical leadership from the AMA and its state and county constituents.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on March 22, 1972. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by an interested member of the Society.*

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Electrocardiogram of the Month:

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

The Significance of the QT and QaT Intervals

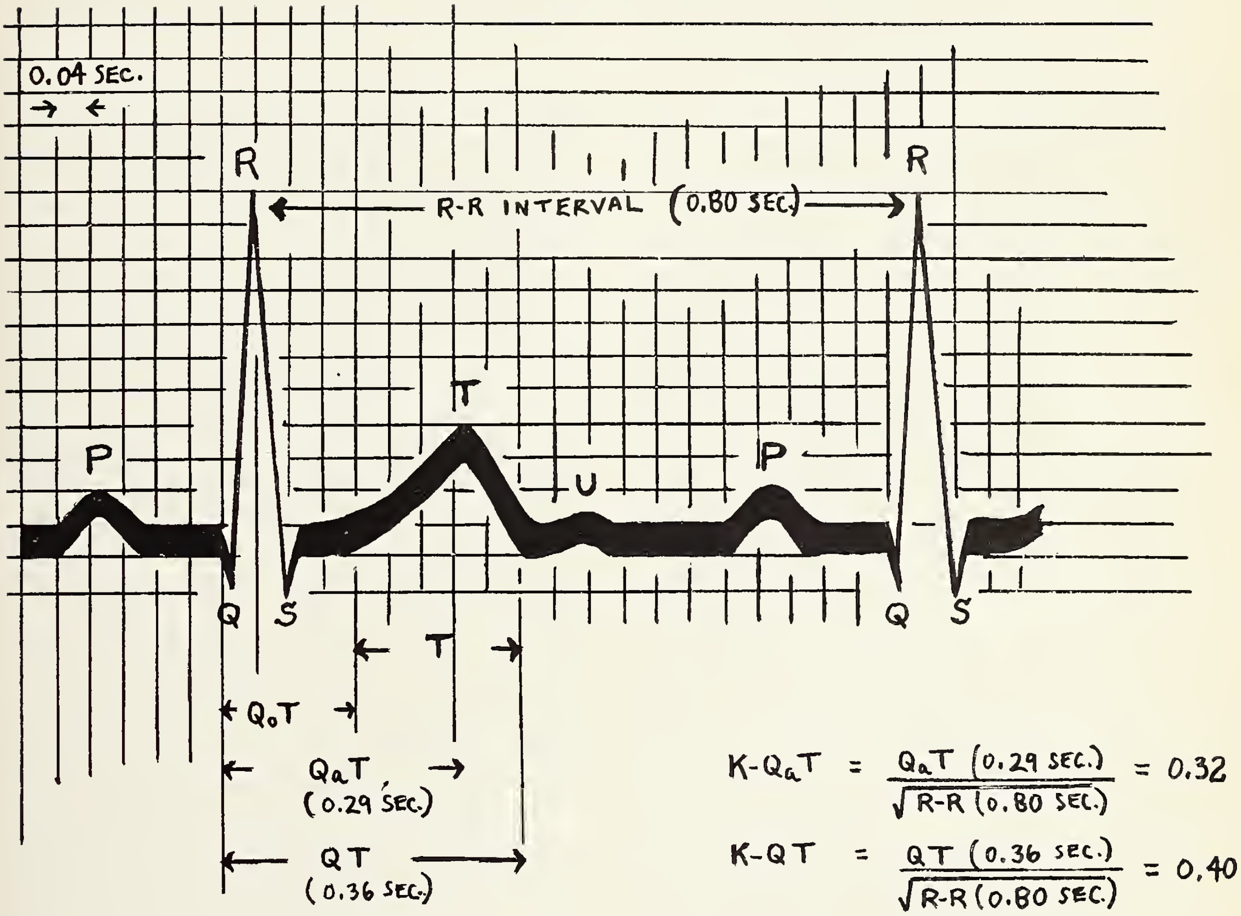
The QT interval in the electrocardiogram (from the onset of Q to the end of T) is a measure of the duration of the repolarization of the ventricular myocardium. Studies on the action potential of single ventricular fibers reveal that there is an initial slow phase of repolarization which corresponds in time to the ST segment and a terminal more rapid phase which corresponds to the T wave. The duration of both the initial and terminal phases can be differently affected by electrolyte, neurogenic, and metabolic abnormalities as well as by various drugs, changes in temperature and alteration in blood supply. It is thus of value to be able to measure the duration of the initial phase and the duration of the terminal phase separately. An approximate measure of the initial slow phase could be obtained from the interval Q to onset of T (QoT). However, this is often difficult to determine because the onset of the T wave may be indistinct. The distance from Q to the apex of the T wave (QaT) is a more easily obtained measurement and is equally useful in determining the approximate duration of the initial slow phase of repolarization. It is advisable to make the QaT measurement in leads in which the T wave is monophasic. The approximate duration of the terminal more rapid phase of repolarization can be obtained from the width of the T wave in leads where the T wave is monophasic.

The total duration of ventricular repolarization, QT, is inversely proportional to the heart rate so that the observed QT and QaT intervals must both be corrected for this variable. Bazett's formula, $\text{QTc} = \frac{\text{observed QT interval (sec.)}}{\sqrt{\text{R-R interval}}\text{ (sec.)}}$ can be used to obtain the corrected QT (QTc). In normal subjects the QTc ranges between 0.35-0.39 in males and between 0.38 to 0.42 in females. The QaT interval can be corrected for heart rate with the formula $\text{QaTc} = \frac{\text{observed QaT interval (sec.)}}{\sqrt{\text{R-R interval}}\text{ (sec.)}}$ In normal subjects the QaTc ranges between 0.28 and 0.32 in males and 0.30 to 0.34 in females.

Fig. 1 illustrates the application of Bazett's formula for obtaining corrected QT and QaT values.

The electrocardiographer can obtain valuable information from a determination of the QTc and QaTc values. The finding of an increased QTc points to the presence of some clinical process prolonging the total recovery period of the ventricles. Conversely, a decreased QTc value indicates the presence of some process accelerating ventricular repolarization. A prolonged QaTc is indicative of a process prolonging either the initial or the terminal phase of repolarization. A prolonged QaTc value in the presence of a T wave of normal duration is indicative of prolongation mainly of the initial phase. A decrease in the QaTc value indicates the presence of a process accelerating the initial slow phase of ventricular repolarization.

(to be continued)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QaT (0.29 SEC.)
QT (0.36 SEC.)
K-QaT = QaT (0.29 SEC.) / √R-R (0.80 SEC.) = 0.32
K-QT = QT (0.36 SEC.) / √R-R (0.80 SEC.) = 0.40

Anesthesiology Grand Rounds
Yale-New Haven Hospital
Placental Abruption with Coagulopathy

Samuel M. Lerner, M.D. and Frederick W. Hehre, M.D., Editors
Jakub Goldstein, M.D., Stewart Stringfellow, M.D.* and Yale Nemerson, M.D.,** Discussants

Dr. Jakub Goldstein:

A 32 year old female, gravida 1, para 0, was admitted to the Delivery Suite at 8:20 P.M. in the 27th week of pregnancy with profuse vaginal bleeding. Blood loss on admission was estimated to be 1000-1500 cc. Admission blood pressure was 120/85 mmHg. During pregnancy her systolic blood pressure had been 150/90 mmHg. Laboratory examination: prothrombin time 0%; fibrinogen 80 mg%; platelet count 137,500 and clotting time greater than 30 minutes. Vaginal examination revealed a closed cervix and brisk bleeding from the uterus. The presumptive diagnosis was premature separation of the placenta and hypofibrinogenemia. After 45 minutes her blood pressure fell to 80/60 mmHg and whole blood was started. In 20 minutes her blood pressure had risen to 120/80 mmHg. She was also given 5.25 gm of fibrinogen, and two hours after admission her clotting time was 5 minutes. Immediate cesarean section was elected. She was considered to have a full stomach, and was intubated awake with a #32 French Megill endotracheal tube. Anesthesia was maintained with 50% N_2O-50% O_2 and 0.1% succinylcholine drip. A dead fetus weighing 475 grams was delivered and a large unclotted hematoma was evacuated from behind the prematurely separated placenta. During operation, she received 3 additional units of whole blood. Blood pressure remained stable throughout the procedure at 110-120 mmHg systolic. At the end of the operation her hematocrit was 31%; prothrombin time 18 seconds (40%); and a fibrinogen 154 mg%.

On the first postoperative day, her platelet count was 92,000. The hematocrit fell to 20% on the fourth postoperative day and she received two additional units of whole blood. On the seventh postoperative day she developed thrombophlebitis of the greater saphenous vein which was treated with heparin 50 mg every four hours, bed rest and leg elevation. The phlebitis improved rapidly, and she was discharged on the 14th postoperative day.

Three months later, the patient was readmitted for persistent hypertension, first noted during pregnancy, but asymptomatic. Blood pressure 150/100 mmHg right arm, 160/120 mmHg left arm. Physical examination was otherwise normal. Laboratory examination: BUN 19 mg%; FBS 100 mg%; cholesterol 130 mg%; and hematocrit 40%; urinalysis negative. Urinary aldesterone level, chest X-ray and electrocardiogram were within normal limits. Retrograde aortogram was normal. Diagnosis of essential hypertension was made and she was started on Hydrochlorothiazide and Reserpine. On the second day she again developed a superficial thrombophlebitis treated with bed rest, hot soaks and dextran.

She was admitted again, 4½ months after the placental abruption, with a two week history of generalized pruritis and five days of progressive anorexia, nausea, fatigue, headache and dark urine. Jaundice was noted on admission. For the past 10 days polyarthralgia had involved the shoulders, knees and hips. Blood pressure 110/80 mmHg. The skin and mucous membranes were slightly icteric, and palmar erythema was present, but without spider nevi. The right upper quadrant was tender,

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DR. FREDERICK HEHRE is Attending Anesthesiologist, Yale-New Haven Hospital.

DR. JAKUB GOLDSTEIN is Attending Anesthesiologist, Yale-New Haven Hospital.

DR. STEWART STRINGFELLOW is Attending Obstetrician and Gynecologist, Yale-New Haven Hospital.

DR. YALE NEMERSON is Attending Physician, Yale-New Haven Hospital.

From the Departments of Anesthesiology, Obstetrics and Gynecology and Medicine,** Yale University School of Medicine and Yale-New Haven Hospital, New Haven, Connecticut.*

but the liver edge was not palpable. The presumptive diagnosis was serum hepatitis, probably acquired from fibrinogen therapy. Laboratory examination: total bilirubin 7.3; direct fraction 4.0; thymol turbidity 12.7; alkaline phosphatase 204 mgs%; LDH 960; SGOT 1140, and prothrombin time 100%. A liver biopsy revealed moderately severe acute viral hepatitis without evidence of subacute hepatic necrosis. Serial liver function tests showed progressive improvement. Nausea, anorexia and pruritis disappeared slowly and the stools became dark. She was discharged on the 13th hospital day.

Patient was admitted for the fourth time 18 months later for elective cesarean section. Her blood pressure had been well controlled with the antihypertensive therapy. Liver function tests were within normal limits. Under spinal anesthesia, cesarean section was performed and a normal 3100 gram boy delivered with Apgar Scores of 9/10. Her postoperative course was uneventful.

Dr. Stewart Stringfellow:

Most cases of abruption occur for unknown causes, but the incidence is three-times higher in women with chronic hypertension and acute toxemia of pregnancy. Blood from necrotic areas in the decidua initiates the hematoma formation. This can be clinically insignificant or result in the ful blown picture of abruption. The incidence varies from one in 85 cases to one in 250 pregnancies. The presentiug symptom may be obvious external hemorrhage when blood dissects between the fetal membranes and the uterine wall and exits from the cervical os or may be concealed hemorrhage confined retro-placentally which separates the entire placenta, causing overdistention of the uterus without vaginal bleeding. The usual presenting symptoms are uterine pain or pressure with or without external bleeding. Since 80% of abruptions are the external type, vaginal bleeding is common. This patient's husband reported impressive hemorrhage at home, and in the car, and her pale face was the picture of impending shock.

On admission the uterus was tetanically contracted, no fetal heart was heard, and on pelvic examination, the cervix was closed. With this picture one would expect hypofibrinogenemia. We observed a blood sample at the bed side which did not clot, and laboratory studies showed severe hypofibrinogenemia. With blood replacement started and fibrinogen given to the point of beginning blood clot, we did the hysterotomy. Hourly urine measurements were followed. Another series of coagulation studies were done to be sure that they were mending, which could be anticipated after emptying the uterus.

I felt compelled to empty this uterus and fibrinogen has stood the test of time. The blood will clot with fibrinogen, which will enable us to empty the uterus safely. In severe abruption when maternal mortality is considered, fibrinogen does have the inherent risk of hepatitis, but it is justified until alternative means of correcting the coagulopathy are effective.

Dr James I. Gilman: What week of pregnancy does abruption of the placenta usually occur?

Dr. Stringfellow: Usually after the 32nd week. The definition of abruption is "separation of the normally implanted placenta after the 20th week". Most abruptions occur in the third trimester.

Dr. Samuel M. Lerner: Dr. Nemerson, please discuss the coagulopathy associated with abruption of the placenta.

Dr. Yale Nemerson:

Pregnant women suffering abruption of the placenta may develop disseminated intravascular clotting and bleed spontaneously and severely. If one could monitor fibrinogen level in this woman, it would drop from normal of 300-400 mgs% to 80 mg%. The half-life of fibrinogen is 3-4 days. If synthesis stopped, no change would occur in a matter of hours; therefore, something has destroyed or utilized it. The commonest cause is the conversion of fibrinogen to fibrin in the ordinary process of blood coagulation. In abruption, placental factors activate the clotting mechanism, and fibrin clots are formed in the retroplacental region of the uterus. The space, filled with fibrin, is an extravascular compartment totally isolated from the vascular spaces, but nevertheless a hemostatic problem develops. Many clotting components are depleted in addition to fibrinogen. Prothrombin time is low, partial thromboplastin time is elevated, Factors V and VIII are depressed. Whenever intravascular clotting occurs, the fibrinolytic mechanism is activated, liberating the proteolytic enzyme plasmin into the circulation. Plasmin catalyses the hydrolysis of fibrin resulting in the release of fibrin degradation products into the general circulation. Fibrin degradation products and deficiencies of clotting factors also cause qualitative and quantitative defects in the blood platelets. Platelets, in the presence of fibrin degradation products, do not form adequate platelet plugs, and fibrin degradation products combine with fibrinogen to form delayed and spurious clots. Although the activation of the clotting mechanism causes decrease in the level of clotting factors, the severity of bleeding is in excess of what one would expect in comparison to congenital coagulopathies with corresponding low levels of clotting factors.

In patients with abruption, placental factors cause intravascular clotting which results in consumption of clotting factors and the release of fibrin degradation products which interfere with platelet function and fibrinogen polymerization. (Figure 1) The resulting hemostatic defect is far more ominous than a congenital coagulopathy.

In the obstetrical patient, one may use fibrinogen and almost turn the process off at will. Deliver the baby, remove the causative factor, the placenta, and the process stops. In the non-obstetrical patient, the treatment of choice is heparin. The hemostatic defect is due to intravascular clotting and heparin is a most effective agent to prevent clotting, and the body wil replace the clotting factors as the fibrin degradation products are cleared by the reticuloendothelial system. Overdosage can be easily corrected by administration of the appropriate antagonist.

Dr. Gilman: Giving heparin for the coagulopathy, what is the chance of further uterine bleeding. In cases other than abruption of the placenta, they do not bleed any more.

Dr. Nemerson: Heparin, in the patient who is bleeding massively with disseminated intravascular coagulation, is a benign drug.

Dr. Stringfelow: It is different since the placental site is going to bleed on a mechanical basis.

Dr. Nemerson: You are really worried about dissection into the uterine wall, aren't you?

Dr. Stringfellow: Yes. Bleeding into the muscle may result in couvelaire uterus.

Dr. Gilman: Is the fibrinogen going to make the uterus contract?

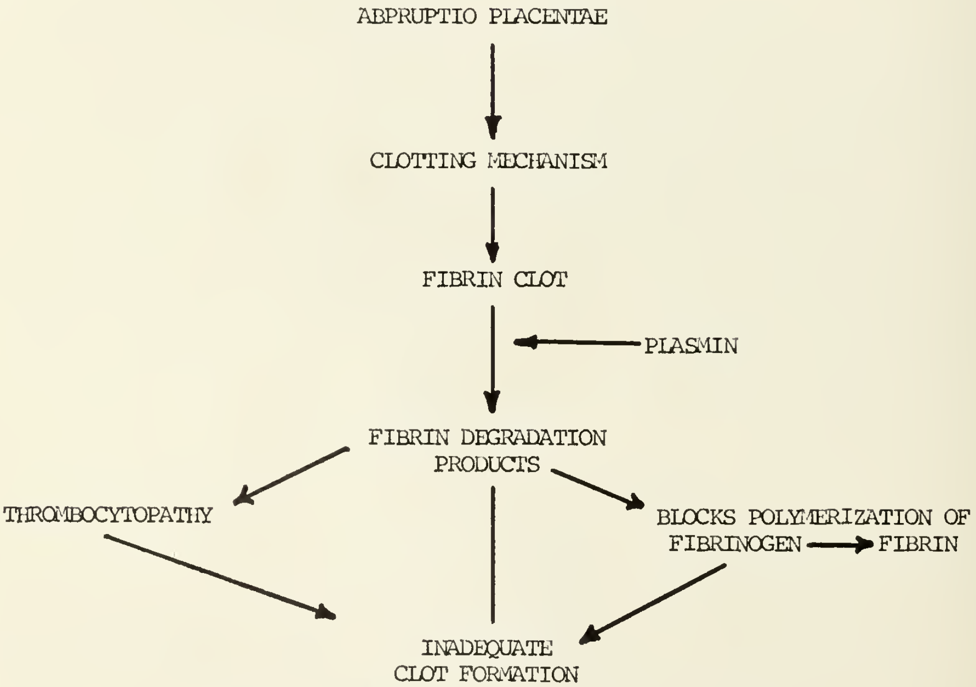
Dr. Stringfellow: Fibrinogen will make the blood clot, but will not stop bleeding into the uterus.

Dr. Gilman: Many people think of heparin dosage of 3 mgs/Kg necessary to anticoagulate patients having cardiopulmonary bypass.

Dr. Nemerson: Patients with disseminated intravascular coagulation use about 250 mgs or 25,000 units per 24 hours, starting with a 50 mg push. This must be reduced in the presence of thrombocytopenia, since platelets neutralize heparin by binding.

Dr. Goldstein: Should gamma globulin be given prophylactically for serum hepatitis?

Dr. Nemerson: The worrisome thing is the subacute hepatic degeneration and death from postnecrotic cirrhosis. Gamma globulin reduces the frequency of icteric hepatitis, but evidence that


ABPRUPTIO PLACENTAE
CLOTTING MECHANISM
FIBRIN CLOT
PLASMIN
FIBRIN DEGRADATION PRODUCTS
THROMBOCYTOPATHY
BLOCKS POLYMERIZATION OF FIBRINOGEN → FIBRIN
INADEQUATE CLOT FORMATION

Coagulopathy Mechanism in Abruption of the Placenta

The appearance of fibrin degradation products interfere with the normal function of platelets and blocks formation of the fibrin clot, resulting in hemorrhage.

gamma globulin reduces the frequency of sub-acute hepatic degeneration and post-necrotic cirrhosis is shaky.

Dr. Gaylord H. Rockwell: In the patient with abruption without evidence of lack of hemostasis, would you treat with heparin?

Dr. Nemerson: We have not treated patients with abruption with heparin therapy here.

Dr. Demetrios Kalas: If 25% of patients receiving 80 gms of fibrinogen develop hepatitis, what is the mortality of this group?

Dr. Nemerson: Under 1%. There are people who have post-necrotic cirrhosis in whom acute hepatitis was never known. Mortality statistics for hepatitis are 95% uneventful recovery, 3-4% delayed recovery and 1-2% with chronic illness or death.

Dr. Lerner: What causes the bleeding defect here? The amniotic fluid debris, tissue thromboplastin or what?

Dr. Nemerson: I do not know what gets out of the placenta, but a tissue factor gets into the circulation.

Dr. Paul G. Barash: If the baby is potentially viable, is the risk to the baby of heparin therapy increased?

Dr. Nemerson: No.

Dr. Frederick W. Hehre: Is heparin indicated in amniotic fluid embolus?

Dr. Nemerson: Yes. Anyone with that severe disseminated intravascular coagulopathy, should be treated with heparin.

Dr. Gilman: What is our source of fibrinogen?

Dr. Nemerson: Fibrinogen is obtained from commercially pooled blood.

Dr. Gilman: Will we screen donors for Australian antigen? It must take huge amounts of processed blood to get 5-8 grams.

Dr. Nemerson: The current figures are that the antibody will detect about one-third of potentially infected bloods, which might be very good for reducing hepatitis transmitted by 3-5 pints of blood.

Dr. Rockwell: Can the concentrates be screened? If they are all positive, why doesn't everybody get hepatitis?

Dr. Nemerson: They will all be positive. If I had the choice of two pints of blood, one at random and one which was Australian negative, I would happily reduce my chances of hepatitis by one-third.

FOR PATIENTS OF ALL AGES, REGARDLESS OF RACE, COLOR OR CREED, WHO NO LONGER REQUIRE GENERAL HOSPITAL CARE AND WANT TO BE HELPED TO "GET UP AND GET WELL FASTER."

SOUND VIEW HAS AN ACTIVE RESTORATIVE AND REHABILITATIVE PROGRAM WHICH IS WELL KNOWN TO THE MORE THAN 150 AREA PHYSICIANS WHO HAVE ADMITTED THEIR PATIENTS TO OUR FACILITY.

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150 Birds

We threw a stone to kill two birds, and got a hundred and fifty.

The two birds were two problems. The first we shared with the county society. A new, inevitable, and admirable county health care plan, providing effective peer review, was a slow starter. Everyone agreed that most doctors would sign up if they understood it.

Second was an auxiliary problem. Younger wives don't join; membership drops. Organizations, just for the sake of being organized, no longer appeal. Country club luncheons and dances are ho-hum. Educated, involved young women demand relevance.

So we thought we could help the men, and catch the women, by educating the wives about the many changes in the air for medicine. We called it a "School Day."

Borrowing from business and psychology, we determined to have two sessions no longer than ninety minutes each, separated by very little food.

We consulted Dr. Ben Wiesel, known as a keep-em-awake, quickwitted, plain-English speaker. The program was mainly his creation.

The county medical association gave us their blessing, the use of their building, and $150 for mailing expenses.

We sent flyers not only to auxiliary members, but to the wife of every doctor in Hartford County, including internes.

There was no charge. Everyone was asked to bring her own brown-bag lunch; coffee was guaranteed.

The speakers, all most gracious, accepted our invitation without hesitation or remuneration.

The day came, it didn't snow, and we had about 150 women, most of them all day but some who came either morning or afternoon. We were pleased to see that many were not auxiliary members, many were young, and all looked alert. They took notes.

In the morning Dr. Wiesel and Dr. Sidney Cramer gave lucid basic instruction covering insurance for hospital care, insurance for doctors' services, Medicare, Medicaid, pre-paid plans, health maintenance organizations, groups, peer review organizations. The new Hartford County plan was made clear.

In the afternoon there was a confrontation among protagonists for various interested parties to health care. Dr. Wiesel moderated.

Speaking for the federal government was Mr. Robert Patricelli, recently Deputy Under-Secretary for Health Planning in H.E.W. For State government was Dr. Morris Cohen, co-chairman of the legislative Committee on Health and Safety. Mr. Daniel Pettengill, vice-president of Aetna Life and Casualty, spoke for insurance. Hospitals were represented by Mr. John Ives, administrator of the University of Connecticut-McCook Hospital. Dr. Paul Lavietes, Medical Director of the New Haven Community Health Plan, spoke on the problems as seen by patients. The doctors had an able spokesman in Dr. Max Goldstein, president of the H.C.M.A.

Each talked for five minutes, and then the questions flew. There seemed to be particular interest in the New Haven plan, among the audience.

All the speakers agreed that our inherited system of health care is creaking, over-burdened, and lopsided. Predictably, they had differing diagnoses and prescriptions for repair.

One high-light was Mr. Ives' statement that for too long physicians, hopsitals, and politicians have been at odds with each other. Now is the time for all these groups to work together to develop a rational, coordinated system of care.

The Hartford County Plan is now off the ground. We hope that we may have helped.

When next our membership applications go out, we'll see if we have met the needs of young wives.

Mrs. Ronald S. Beckett
Bloomfield, Conn.
Legislation Chairman-Hartford County

PUBLICATION OF WEINERMAN MEMORIAL VOLUME ANNOUNCED

The *Yale Journal of Biology and Medicine* announces the publication of the hard cover edition of its *Weinerman Memorial Volume, Selected Papers and Contributed Articles on Health Services* of the late E. Richard Weinerman, Professor of Public Health and Medicine, Yale University School of Medicine.

This special volume of the *Yale Journal,* originally published in August, 1971, is dedicated to Professor Weinerman, whose accomplishments before coming to Yale and since have added substantially to knowledge of the disciplines of medical care and health services administration. Early in his professional life, Dr. Weinerman set himself on a course toward study and understanding of how the physician and his socially concerned colleagues could serve better the individual patient, the whole family and all society.

Dr. Weinerman, and his wife and co-worker Shirley Basch Weinerman, were among the victims of an act of sabotage that blew up the plane in which they were traveling from Switzerland to Israel on February 21, 1970. They were on their way to Israel, then New Zealand and Japan, to continue international comparative studies of medical care delivery systems.

This publication is an attempt to restate some of E. Richard Weinerman's ideas and concepts before time blurs their context and their meaning. In the present and future national striving for change to improve the health care system his suggestions have much relevance, and deserve implementation. In addition to reprints of a selected group of writings by Dr. Weinerman, previously published during a span of 20 years, this volume includes two previously unpublished but significant papers by Dr. Weinerman. One is an evaluation of three group medical clinics in the Pittsburgh area, clearly outlining a rational approach to parameters of the quality of medical care. The other represents the summation of many months of deliberations with a committee of medical care experts on the strategy of incorporating incentives for changing the traditional medical care system in legislation for a national health insurance program.

This special volume is available from David A. Pearson, Ph.D., Department of Epidemiology and Public Health, Yale University School of Medicine, 60 College Street, New Haven, Connecticut 06510. The $10.00 price is a tax deductible contribution to the "E. Richard and Shirley Basch Weinerman Memorial Fund," a charitable, tax-free fund for the support of research efforts by students of the Yale University School of Medicine in social medicine and community health care developments, with emphasis on minority student support and programs of health care for disadvantaged communities.

Stephen Fleck, M.D.

In Memoriam

Gager, John J., Tufts University, 1942. Dr. Gager was head of the department of ophthalmology at Lawrence Hospital and a practicing ophthalmologist in the New London area since 1943. He was a member of the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Gager died February 9, 1972, at the age of 56.

Rafferty, Brae, Jefferson Medical School, 1928. Dr. Rafferty was a surgeon in the Windham area since 1930. Dr. Rafferty served as chief of surgery at Windham Hospital from 1943 to 1945 and in 1962 was president of the medical staff. He also served as president of the Windham County Medical Association in 1937, and president of the Connecticut State Medical Society in 1951. He was also a member of the American Medical Association. Dr. Rafferty died February 16, 1972, at the age of 70.

Shortening The Medical Curriculum

(*Science* 174:1303, 1971). In a recent issue of *Science* Professor De Witt Stetten has raised some well founded objections to the issue of reducing the medical curriculum to 3 years.

He thinks an increase in the number of physicians will not significantly combat the health care crisis unless health services are improved. Shortening the curriculum will provide only one additional class of graduate physicians.

Increasing the size would do more over a longer period to increase the output. This would cause temporary accommodation problems that could be overcome as regards laboratory and classroom space. But the availability and tolerance of patients especially if the shift system is adopted is questionable.

Important questions are raised by Dean Stetten about the quality of education provided in a 3-year course. For instance, could the student cope? War experience throws some doubt on this. The amount taught would have to be reduced.

Laboratory courses and research exposure will inevitably suffer and so too will vacation time. More intensive teaching may tend to reduce habits of private study which are difficult enough to encourage in a 4 year course.

Instances like these need to be thought about now.—L.H.N.

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Allergist—Wanted as soon as possible. Must be board eligible for a two-man allergy practice which now requires a third man. Work week is four days; every third weekend off. Early partnership for right man guaranteed. 100,00 population. Centrally located in a university town. Connecticut license required. First year-five figure salary. Area Code 203 346-1575.

Anesthesiologist—To join three man group in 180 bed community hospital. Interest in inhalation therapy and respiratory physiology important. Recent or near future residency graduate acceptable. Living conditions excellent in semi-rural area with nearby University of Conn. and State College affording many recreational and cultural advantages. Please contact Anesthesia Associates, P.O. Box 23, Willimantic, Connecticut 06226. Tel. 423-9201.

Anesthesiologist—To join Board certified chief of anesthesiology in small community hospital. No OB. Salary negotiable. If interested contact administrator or chief of anesthesiology. Johnson Memorial Hospital, Stafford Springs, Connecticut 06076.

Anesthesiologist—Associate position in medium sized community. Centrally located.

Chest Physician—needed for clinic.

Connecticut Based Insurance Company: Three physicians needed: Employee Health Clinic; Claims Review; Medical Evaluation for Underwriting Purposes. Connecticut license. Good benefits.

Director of College Health Service—Full time position; September, 1972; C. B. Crampton, M.D., Wesleyan University, Middletown, Connecticut 06457.

Emergency Room Physician—To complete four-man group. 100-bed, full service hospital. Solid backup in all specialties and most subspecialties from Active Staff. Central Connecticut community midway between Hartford and New Haven. Must be eligible for Connecticut licensure. Attractive salary, excellent benefits. Resumé to Chief of Staff, World War II Memorial Hospital, Meriden, Connecticut 06450.

Family Practice—North Branford, All America City, suburb of New Haven, requires family physician to establish practice. No other physician at this time. Contact Irving H. Beck, Town Manager.

Family Practice—Southwestern Litchfield County. Community hospital. Conveniently located. Community physicians also searching for pediatrician and Ob/Gyn to enter private practice.

Family Practice—Growing community seeks family physicians. North-central Connecticut. Approximately 47,000 population. Several hospitals in the area. New hospital in planning stages. Number of specialists in town. Conveniently located.

General Practice, Internal Medicine, Ob-Gyn and ENT: Needed in town of Torrington. 200 bed hospital. 50 physicians, over 50,000 population, Contact Joseph F. J. Curi, M.D., Chairman of Search Committee, Charlotte Hungerford Hospital, Torrington, Connecticut 06790. 203-482-0441.

General Practice and Internal Medicine—Both for solo and hospital based practice. Medium sized, north central community. Community hospital. Needed immediately.

General Medicine and Internal Medicine—Northwestern Connecticut community seeking to attract practitioners. Associate type practice possible.

Insurance Company Physician—Young physician needed to assist in underwriting, claims and employee medicine.

Internist—A third Internist is needed to join two other Internists in the town of Manchester, Connecticut. Office located across the street from a 300 bed community hospital which is currently in the second of a three stage building program. Manchester is located fifteen minutes from Hartford, one hour from New Haven, one hour and a half from Boston and two hours from New York City. For further information contact: Harold J. Lehmus, M.D., or David L. Warren, M.D., 56 Haynes Street, Manchester, Connecticut 06040. Telephone: 203-646-1167.

Internist—Preferably Board Certified or eligible, for chronic disease and cancer hospital having sections for TB in adults and children. 35 hr. week, 11 paid holidays, sick leave, 3 weeks vacation after one year of service. Salary level: $23,227-28,333. Paid health insurance and minimum charge for life insurance. Apartment available for physician with small family. Write Medical Director, Uncas-on-Thames Hospital, Norwich, Connecticut 06360.

Ob/Gyn—Community in western Connecticut in search of physician to open private practice. Community's growth requires additional medical services.

Ophthalmologist—Associate needed to join two other ophthalmologists in large, centrally located Connecticut city.

Otolaryngologist—Two physicians approaching retirement. Eastern part of the state. Coastal area.

Pathologist—Chief of Pathology wanted for 100 bed, full service community hospital. Excellent lab facilities, well staffed and equipped. Fee for service or salary. Central Connecticut. 20 minutes to either Hartford or New Haven. Resumé to Chief of Staff, WW II Memorial Hospital, Meriden, Connecticut 06450.

Pediatrician—Community physicians feel that another pediatrician is needed. Central section of the state. 40% of population 18 years of age and under.

Pediatrician—currently board-eligible or board certified. Full-time position. Salary negotiable. To practice family oriented medicine in a private, non-profit neighborhood health center. For further information please contact Evans H. Daniels, Jr., M.D., Medical Director, Community Health Services, Inc., 1023 Albany Avenue, Hartford, Connecticut, 06112. Telephone 549-1423.

Proctology—Lucrative practice available in New Haven. Physician deceased. Fully equipped office. Contact: A. M. Murray 203-787-4161.

Radiologist—Large hospital needs radiologist.

Senior Physician—positions available at Norwich Hospital. Primary responsibility for medical care of geriatric and mentally ill patients in a community oriented, geographically unitized hospital with many forward looking, exciting programs. Starting salary $20,465, many fringe benefits, hosuing available. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT

BOOK REVIEW

EYE SYMPTOMS IN BRAIN TUMORS, by Alfred Huber, M.D., 2nd edition, translated by Frederick C. Blodi, M.D., The C. V. Mosby Co., St. Louis, 1971, 376 pp. illus. $32.50.

Reviewed by: HARRY H. MARK

Neuro-ophthalmology is one of the few areas where the patient's life itself often depends on the vigilance of his eye doctor. Newer radiographic techniques of detection coupled with advanced microsurgical and radiation modes of treatment helped improve the prognosis for the patient with a brain tumor. But early clinical diagnosis is still a decisive determinant in this prognosis.

The ophthalmologist's role is underlined by the fact that about 60% of the 2500 patients examined had ocular symptoms among the initial complaints in a brain tumor. In 25% of tumors near the visual pathways a fairly accurate localization could be made by ophthalmic means alone.

Since about 60% of patients with brain tumors had papilledema, it is not surprising that almost a fifth of the book is devoted to this subject. Differential diagnosis has been aided by the newer method of fluorescein angiography, balancing a possibly increased incidence of pseudopapilledema, such as from corticosteroids.

Defects in the visual fields are another manifestation of brain tumors. To do good fields is often a frustrating and time consuming task, which nevertheless remains crucial to documenting early evidence and later progression of brain lesions. The utility of visual-field examinations has recently been enhanced by the addition of new instruments, such as the Harms-Tübinger static perimeter and Goldmann's perimeter with its auxiliary attachments.

All these methods and more are fully described and illustrated in the book. Their beneficial application in practice is made convincingly clear by numerous case reports. The flowing language is eminently readable, attesting to the writer's and translator's lucidity of thought. The 233 line-drawings, photographs and radiographs are sharp and to the point. There are abundant references to the literature, with a long and modern bibliography, and a fairly comprehensive index.

Some of the chapters may seem somewhat short, as for instance those on exophthalmos or aneurysms. Some interpretations of clinical evidence, such as nystagmus, may also be subject to controversy among experts, as is perhaps inevitable for a book written by a single author from personal experience. Exception to the proof-reader's care is figure 1-14 (taken from Kestenbaum), where internal rotation (adduction) is substituted for external rotation, and vice versa.

All in all, this is a most important book, superbly organized, written and illustrated. It is indispensable to the ophthalmologist who wishes to avoid the fatal error of prescribing glasses instead of a craniotomy. It would also benefit neurologists, neurosurgeons, and others concerned with brain tumors, not the least by acquainting them with the capabilities of modern ophthalmic methods supplementing their own.

Pre-Sate® **(chlorphentermine hydrochloride)**
Caution: Federal law prohibits dispensing without prescription.

Indications
Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (i.e. several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications
Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings
When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.
Drug Dependence Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with the high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.
Usage In Pregnancy The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.
Usage In Children Not recommended for use in children under 12 years of age.

Precautions
In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug Psychologic disturbances have been reported in patients who concomitantly receive an anorectic agent and a restrictive dietary regimen.

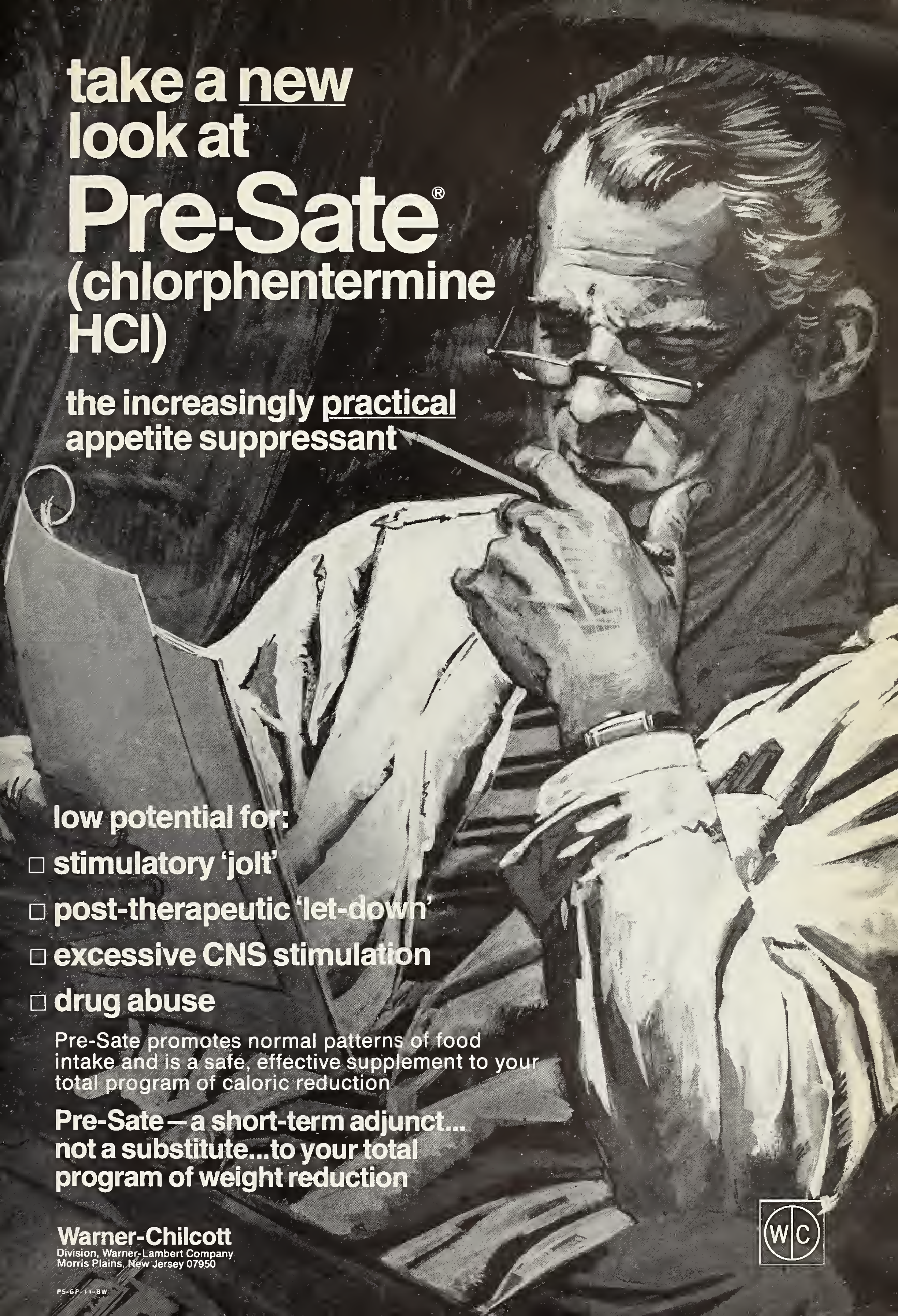
Adverse Reactions
Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration
The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage
Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.
Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied
Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

Full information is available on request.



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Placement Wanted

In the past month the Placement Service has received a great number of resumes from physicians interested in locating in Connecticut. Many will be completing in the summer their residency and/or their military obligations. Space does not permit us to list each candidate separately. Please refer to the following listing and contact the Placement Service for more information. (865-0587)

Allergy—Three Board certified or Board eligible candidates have resumes on file.

Anesthesiology—Five candidates have indicated interest in locating in Connecticut. Two with Connecticut licenses.

Dermatology—Three have submitted resumes. One Board eligible; one Board certified.

Family Practice—Twelve have submitted resumes for consideration.

Internal Medicine—Fifty-four resumes are on file. Many sub-specialties.

Neurosurgery—Five candidates have indicated interest in settling in Connecticut.

OB/GYN—Two resumes are on file. One Board certified; one Board eligible.

Opthalmology—Twelve resumes are on file. Most will be available in July.

Orthopedics—Nine have submitted resumes for placement in Connecticut.

Otolaryngology—Four resumes are on file. One with Connecticut license.

Pathology—Eight have indicated interest in locating in Connecticut.

Pediatrics—Eleven have resumes on file.

Psychiatry—Seven have indicated interest in locating in Connecticut.

Radiology—Five have resumes on file.

Surgery—Thirty resumes are on file. Many sub-specialties.

Urology—Nine have indicated interest in Connecticut communities. Eight are Board Eligible; one Board certified.

Allied Personnel

EEG Technologist—31 years of age. Nine years of experience. Wishes position as instructor in clinical EEG Technology or technologist in charge of new laboratory. Available June 1. Presently at University of Kentucky completing degree program. Richard F. Wilmarth, 133 Brown Avenue, Lexington, Kentucky 40505.

Physician's Assistant—30 years of age. Presently enrolled in Physician's Associate Program at Duke University. Available September 1972. Desires position with general practitioner, pediatrician or internist in solo or group practice. Ralph B. Lenoci, 261 King Street, Port Chester, New York 10573.

Business Manager—College graduate; 13 years administrative experience in clinic, hospital and health care fields. Available within 30 dasy. Irven V. Roberts, 85 Prescott Street, Torrington, Conn. 06790. 482-8398.

Dermatologist—American Board Certified; Connecticut License; Interested in Group, Associate or Institutional Practice in large or medium sized Connecticut community. 31 years of age. Nira R. Silverman, M.D., 91 Corbin Road, Hamden, Connecticut 06517.

Family Practice—28 years of age. Interested in group practice. Available mid-1972. Arthur L. Stein, M.D., 1117 Grant Boulevard, Syracuse, New York 13203.

General Practice—Connecticut license. Prefers solo practice. 50 years of age. Available immediately.

General Practice—28 years of age. Solo, group or associate practice. Connecticut license. Large or medium sized community. One year of residency in surgery. Arthur E. Woolfson, M.D., 33 Highland Street, New Britain, Connecticut.

Radiologist—Holds Connecticut license. Temporary coverage effective April 21, 1972. Trained for the past four years in London. Danniel P. McCarthy, M.D., 1, Holyoake Walk, Ealing, London W5, England.

Summer Employment Opportunities: Camp physicians; part time or vacation coverage. Medical students seeking hospital or laboratory positions. Contact: Connecticut State Medical Society—203-865-0587.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

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Meeting Notices

The information on this "notices" page is offered as a service of all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the month preceding date of issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

GENERAL

September, 1971-May, 1972
Lecture Series—Each Tuesday
Basic Sciences As Related to Clinical Medicine: Infectious Diseases, Coronary Care Problem, Diagnosis and Treatment of Tumors
Lawrence and Memorial Hospitals
New London, Connecticut
Contact: Edward Gipstein, M.D.

June 12-16—Monday-Friday
5th Conference on The Clinical Delineation of Birth Defects
Johns Hopkins Medical Institutions
Baltimore, Maryland 21205

CARDIOLOGY

May 11-12—Thursday-Friday
Eight Annual Cardiovascular Symposium
St. Francis Hospital—Hartford
Contact: Robert M. Jeresaty, M.D.

June 8-11—Thursday-Sunday
Cardiac Arrhythmias
Virginia Beach, Virginia
Contact: Charles L. Baird, Jr., M.D., Medical College of Virginia, Richmond, Virginia 23219

IMMUNOLOGY

May 8-12—Monday-Friday
Clinical Immunology
McGill University—Montreal

INTERNAL MEDICINE

May 15-19—Monday-Friday
Neurology and the Internist
Cornell University Medical Center
New York City

OCCUPATIONAL HEALTH

September 11-12—Monday-Tuesday
32nd Annual AMA Congress on Occupational Health
Drake Hotel—Chicago, Illinois

PULMONARY PHYSIOLOGY

October 22-25—Sunday-Wednesday
Clinical Pulmonary Physiology
Poughkeepsie, New York
Contact: New York Trudeau Society, Room 710, 105 East 22nd Street, New York, New York 10010

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Neurohypophysial Hormones. Ciba Foundation. In honour of Professor Hans Heller. Edited by G. E. W. Wolstenholme and Joan Birch. Churchill Livingstone, Edinburgh and London, 1971. pp. 139.

Strategy Of The Viral Genome. A Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Churchill Livingstone, Edinburgh and London, 1971. pp. 394.

Lactogenic Hormones. A Ciba Foundation Symposium in memory of Professor S. J. Folley. Edited by G. E. W. Wolstenholme and Julie Knight. Churchill Livingstone, Edinburgh and London, 1972. pp. 404.

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Connecticut Medicine

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Connecticut State
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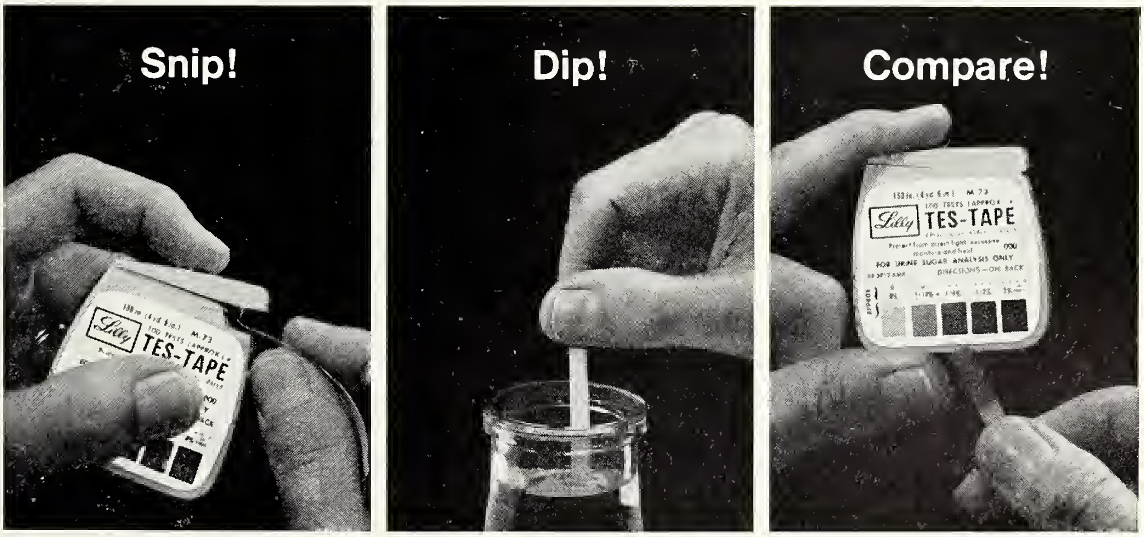

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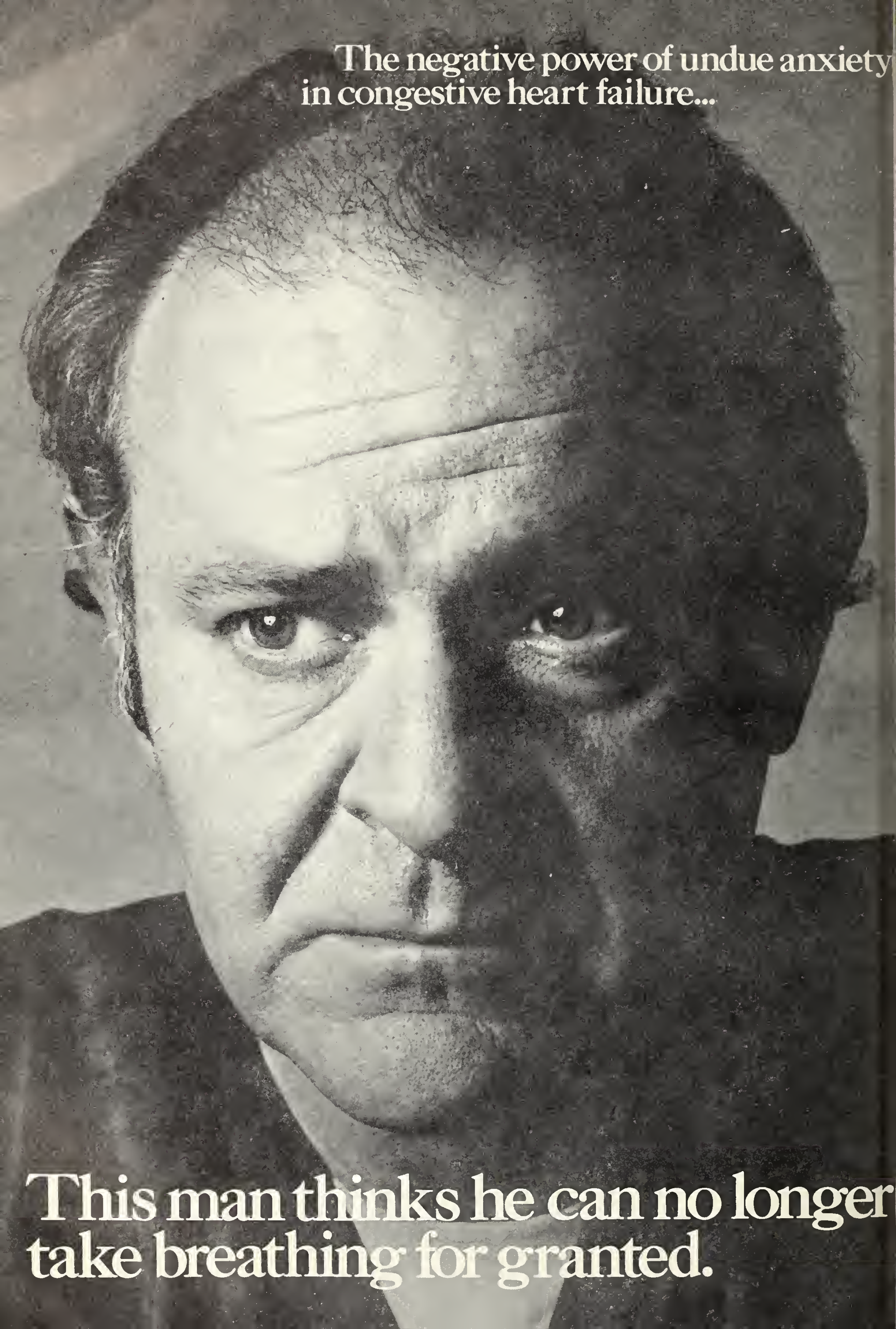
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MAY, 1972
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PRESIDENT'S PAGE

It is with mixed feelings that I look forward to the ensuing year as president of the Connecticut State Medical Society. On the one hand there is the pride and pleasure attendant on having been chosen to assume this high office. On the other, there is the realization of the responsibilities and work entailed, at a time when it seems as though the demands on a physician's time are increasing by geometrical progression.

It is a cliche to say that these are troubled times, but as far as health care and medical practice are concerned, these are *indeed* troubled times, with a threat of far-reaching and rapid change. This is no time for complacency or apathy on the part of physicians. Changes will take place—and are taking place—with or without the involvement of physicians individually or collectively. What form these changes will assume is still not clear, and it is, in part, the fear of the unknown which tends to have a paralyzing effect, and makes "business as usual" seem like an attractive alternative. It is, however, not really a viable alternative in the face of inevitable change. As physicians we should not dread change, since we know it to be a normal element of life and of social organizations. But change should be evolutionary and orderly or it will lead to chaos. To the extent that we may, we should exert every effort, not to prevent change, since this would be fruitless and self-defeating, but rather, with the expertise which is the singular talent of physicians, to guide the direction in which change will occur. As individuals we may exert that influence in our everyday practices, in our continuing efforts at self-improvement, and in our ability to convey our attitudes directly to our patients.

Gertrude Stein said 'one and one . . . is a hundred.' This is certainly true. But equally true, is that by uniting as physicians, we develop increased power through numbers. This is no time for physicians to stand aloof on the sidelines, disapproving of 'organized medicine'. We have enough non-medical critics. Now is the time for physicians to become involved, to help guide the leadership of organized medicine in its sincere desire to reflect the wishes of physicians with respect to the position we should take concerning the changing aspects of the practice of medicine.

While there are many widespread rumors and predictions, they are just that —rumors and predictions. No one really has any hard facts, and the best informed believe that a pluralistic health care delivery system will prevail for the foreseeable future. The specific form or system which best suits the needs of a community will, in an open market place, survive. And those needs should, and probably will be determined on a community, rather than on a national level. Any attempts to establish a federally determined monolithic health care system for the entire country will fail.

But whatever changes the future holds, we, as physicians must continue to give good medical care to our patients, and must become more involved in the process of changing patterns of care, rather than to permit this area to become the private preserve of planners and politicians.

David A. Grendon, M.D.

DAVID ARTHUR GRENDON, M.D.

President

Born New York City, June 9, 1903

College of the City of New York, B.S. 1924

Harvard Medical School, M.D. 1928

Internship, Bellevue Hospital, New York City, 1928-30

Residency, Pondville Hospital, Walpole, Mass., 1930

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Medical Staff, Bronx Hospital, 1935-41

Instructor, College of the City of New York, 1931-41

Instructor, Queens College, 1938-41

Lt. Col., AUS, 1941-46

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Radiologist, Sharon Hospital, 1947-

Radiologist, Fairview Hospital, Great Barrington, Mass., 1951-71

Consulting Radiologist, Fairview Hospital, 1972-

Consulting Radiologist, Wassaic State School, Wassaic, N.Y., 1948-

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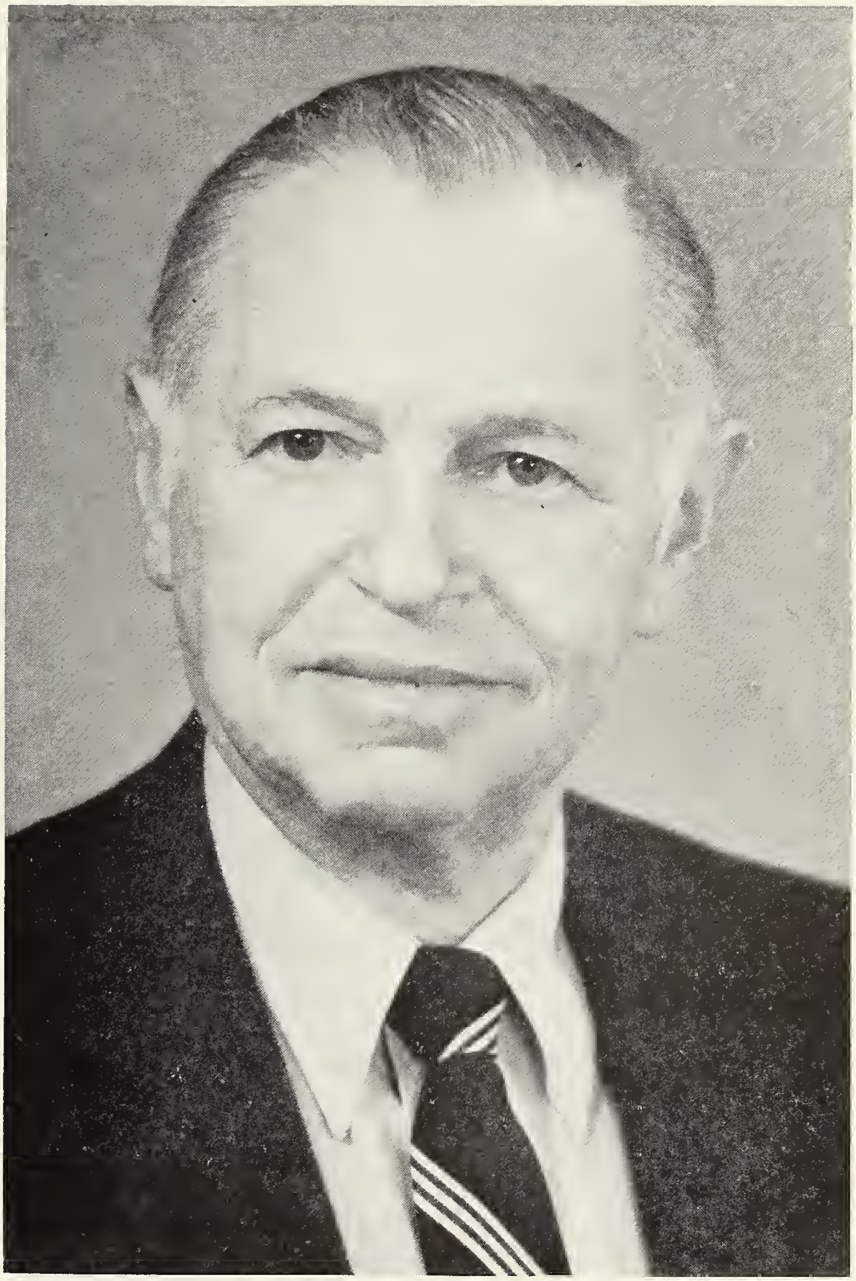
Diplomate of the American Board of Radiology

Treasurer, Connecticut State Medical Society, 1966-69

Vice President, Connecticut State Medical Society, 1970

Councilor, Litchfield County Medical Society, 1958-1966

Board of Directors, Connecticut Hospital Planning Commission, 1968-



DAVID A. GRENDON, M.D., *President*

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In fact, Doctor, you are urged to offer suggestions for future topics. They would be warmly welcomed by the editorial board.

These leaflets are offered at cost to members at $1.00 per hundred, postpaid, in multiples of one hundred. You may use the form below to inform us of your initial requirements.

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Foreword

Fifty Years of Milford Hospital

Mr. Robert Beard

By the year 1920, Milford which for many years had been a sleepy little community, boasted of a population of more than 10,000 and with its growth and progress came its problems, not the least of which was traffic, especially on heavily traveled U.S. Route 1.

Many serious automobile accidents caused grave concern among local residents and especially the local medical profession who were alarmed at the lack of facilities to treat accident victims who had to be transported to New Haven or Bridgeport.

In June of 1920, Charles Beardsley, 91, and the town's oldest resident, was approached regarding 3.5 acres of land he owned a few blocks from Milford center and on which stood the 265-year-old Stockade House.

The property which was valued at $25,000 was offered to the Medical Society. Thus, the first Milford Hospital was established. Since Milford Hospital was to be a privately owned and non-profit corporation, a fund-raising effort and subscription drive were launched, with pledges to be payable in three installments. Citizenry were slow in responding, so with only one quarter of the needed funds pledged after three months, the hospital society considered renovating the Stockade House instead of erecting a new building.

Renovation efforts quickly got underway with private rooms, men's and women's wards, a maternity ward and nursery, a "etherizing room," operating room, nurses' room and dining room, kitchen and bathroom the goal.

A week before Christmas, 50 women from the community formally organized a Hospital Auxiliary. They would meet every week to make 30 pairs of curtains and do all the necessary sewing required by the hospital.

By January 15, 1921, the renovated Stockade House was ready. On January 17, 1921, Milford's first patient was admitted and during the first week there would be ten others. Rates for private rooms were $21 per week.

Accident victims and surgical patients quickly outgrew the 15 beds and nurses were forced to utilize two rooms in an adjoining home and since the Stockade House had no elevator, patients had to be carried to the second floor operating room on an outside stairway.

With the need for a permanent hospital, a new fund drive was launched. Plans for the new building went full steam ahead and by June 2, 1923, a cornerstone was laid for the first permanent building, to cost $65,000. The two-story red brick building when completed the following March contained 25 beds. The Stockade House was converted for use as a nurses' home.

MR. ROBERT BEARD, President of the Milford Hospital Association.

Milford's population was steadily growing and by 1935 additional facilities were needed and more beds were added. Another addition was erected in 1953. This new wing included two operating rooms, a central supply area, sterilizing room, X-ray room, clinical laboratory and accident and fracture rooms.

Still another addition was erected in 1958 following an ambitious fund drive which raised $400,000. This addition included two floors and a basement containing a boiler room, generator, and a transformer. The Memorial unit including two 20-bed medical and surgical floors equipped with piped in oxygen and suction and a basement with an emergency generator and assembly hall and lounge was built in 1960.

In 1963, a lab was opened in an addition which also housed a modern dietary department and obstetrical department of 20 maternity beds and three nurseries and three delivery and labor rooms. With this addition, the hospital's bed patient total reached 120.

In 1971, a new addition costing 3.2 million dollars was completed. 50 years later and with a population of 50,000 Milford now has a hospital with 150 beds, 5 operating rooms, a pathology department, an emergency room that will treat 25,000 patients in 1972, and a medical staff of over 50 physicians.

Milford Hospital is governed by a board of directors elected annually. It is a service institution which must depend on patient fees for the bulk of its revenue with only a small percentage of added revenues derived from fund-raising effort and community support.

The Patient

My anxiety is that today, with the continuing shortage of doctors, the increasing complexities of medicine and surgery, the inevitable change in doctor-patient relationships brought about by the National Health Service, and the influence of other pressures in modern society, we are in danger of losing sight of the precious heritage of respect for human dignity and consideration for the individual for which British medicine is so deservedly renowned.

It is surely a sad reflection on the medical profession in Great Britain today that there should be a place for a flourishing organization known as 'The Patients' Association', the stated purpose of which is to safeguard the rights and dignities of those entrusted to our care!

That well-known prayer composed by the late Sir Robert Hutchison touches on the subject: 'From inability to let well alone; from too much zeal for what is new, and contempt for what is old; from putting knowledge before wisdom, science before art, and cleverness before commonsense; *from treating patients as cases*; and from making the cure of the disease more grievous than its endurance, Good Lord deliver us!"

K. F. Stephens
'Patientese': some thoughts on pre-operative
and post-operative patient psychology.
Proceedings of the Royal Society of Medicine
64:883-885, 1971

Milford Hospital Fifty Years Ago and Today

Waldo E. Martin, M.D., Guest Editor

(1) In 1920 Milford's population was 5,000—now it is 50,000. The first Milford Hospital was established on its present site by a gift of 3½ acres from the Beardsley family. Plans for a permanent Hospital were born. Plans were drawn by a local architect, Walter J. Skinner, free of charge. Then came the fund raising effort, subscription drive and its slow response of citizens. However, by Jan. 15, 1921 the renovated Stockade House was ready.

512 visitors brought gifts of food. On Jan. 17 1921 Milford Hospital's first patient was admitted. 10 others came in that week and the rate was $21.00 for a private room per week.

The Fire and Police department injured or rendered ill in line of duty were treated free of charge. The latent altruism of medicine shines clearly through this item.

(2) By the end of March, 9 babies were born at the Milford Hospital, all of them boys and 1 twin.

(3) Accident victims and surgical patients quickly outgrew the 16 bed hospital and an adjoining building was added.

(4) It is now apparent a permanent hospital was needed and by June 2, 1923 the cornerstone was laid for the first permanent building to cost $65,000. The two story brick building had 25 beds and the Stockade House became a nurses' dormitory.

(5) Milford population was growing and another addition was erected in 1953—

(a) It included two operating rooms and central supply area, sterilizing room, X-ray equipment, accident and fracture rooms.

(b) This was not enough and another addition in 1958 at a cost of $400,000 was built.

(c) In 1963 a laboratory was opened, dietary department, obstetrical department with 20 beds, three nurseries, and delivery rooms. The Hospital now had 120 beds.

(d) This new addition is the most ambitious, and there will be 30 new beds, modern surgical, pediatrics, X-ray and emergency rooms, a new lab and intensive and coronary care unit. It is in fact a real community hospital providing round the clock medical care and emergency treatment to residents of the community and surrounding area. Milford Hospital is a "Hospital with a heart". The reason it is true is that human life is our most priceless possession and the medical profession is dedicated to the philosophy that it works in the best interest of the patient. It dedicates itself in the service of humanity and operates on the precept taken from the Talmud that he who saves a life saves a whole world.

What did we physicians know in 1921—

1. The only drugs we had were simple anesthetics like Ether, barbiturates, salycilates, quinine, morphine and digitalis. Apart from good food, nursing and hygiene, we were able to do almost nothing for infections, blood diseases, high blood pressure, heart disease, stroke, cancer, diabetes and most other disorders.

(2) Today the techniques available to the medical profession for saving life have become increasingly powerful. There is no doubt that in the course of an ordinary week's work the doctor will save lives of an appreciable number of people. The terrors of childbirth and of surgery have vanished, the infectious diseases, the baby with pneumonia, the child with meningococcal meningitis, the young adult in a car accident would all face certain death were it not for the corpus of knowledge possessed by the profession. High blood pressure which used to kill and invalid when this hospital was young is now under control. So is diabetes, some types of cancer and much more.

3. The advances in surgery are phenomenal. We can now operate on lungs, heart, brain with immunity and with success. We can probe in every area of the body to detect and often cure obscure ailments. We can screen for multiple silent disorders and find them before full-blown diseases become manifest.

4. All of this can and will be done in this Hospital by highly qualified physicians and laboratories that will serve our Hospital and community. Our emergency service is as good as any in the state and probably better than the University Hospital. For there it is manned by internes and residents. Here it is manned by our own experienced and seasoned staff. They know how to separate the psychological from the physical component of diseases and most

of our emergency room patients leave with a loss of anxiety and fear, and are relieved.

In a community Hospital such as ours we have the interface between society and medicine. People must remember that many of the problems thrust upon us physicians are of social origin.

> Deaths from carbon monoxide due to obsolete space heaters, refrigerators and smoking.
> Deaths from lead paint.
> Deaths due to improperly fashioned automobiles.
> Deaths due to alcoholic drivers.
> Deaths due to illness from drug abuse, from hepatitis coming from tattoo parlors.
> Illness from unsafe foods.
> From illegal abortions.
> From improperly designed highways.
> From poorly ventilated factories.
> From exposure to toxic materials and dusts.
> From venereal disease.

are but a few of the many societal illnesses which if controlled could greatly reduce the burden on physicians and hospital beds.

As benefactors of the Hospital you should know the role of society in illness and some of you should become leaders in solving problems that would reduce the need for physician and hospital care as well as helping to make the physician's opportunity for prevention and care of disease optimum.

We physicians on the other hand dedicate ourselves to continue to grow as medicine grows, to render ourselves increasingly expert in applying the newest and best knowledge that becomes available in the treatment and cure of illness and the preservation of human life and health. This new Hospital you have given us is the instrument to help us render our service to humanity. It stands as a monument to community dedication to the benefit of all humanity.

The Oath of Geneva which every physician takes on graduation is that we dedicate ourselves to serve in the best interest of our patients and in the service of humanity. This new Hospital which you have given us shows that you are helping the physician realize his obligations undertaken in the Oath. Together we will strive to add quality to life so that man can realize his highest potential.

The William Fischer Lectureship

Louis H. Nahum, M.D.

This memorable occasion of celebrating the Jubilee of Milford Hospital is also the occasion of the annual Wm. Fischer Lectureship. It is appropriate to ask the question why we have undertaken permanently to honor this physician.

He never wrote a scientific article. He never did research work in Medicine. He never gave learned lectures to learned societies. Yet many such are forgotten but Bill Fischer remains and will remain as long as Milford remains and the Milford Hospital remains for it is he who built this permanent monument dedicated to the public but also to the profession. Just think of what our profession would be today without a hospital.

Bill came to medicine a little late since he was an accomplished pharmacist before entering medicine. He soon became the leader in medicine in the community and in the councils of the County and State Society.

A new oath is being taken by the physician, the oath of Geneva, in which a physician dedicates his life to serve the best interest of his patient and in the service of humanity. Long before this, Dr. Fischer already was serving in the best interest of his patient but also dedicating his life in the service of humanity.

> He had a simple philosophy—
> that life is better than death and he strove to preserve life—
> that health is better than sickness and so he organized the public health department in Milford and manned it—
> that an important human goal is that of possessing the state of person, of human dignity.

This means that he treated human beings as ends in themselves and not as means, that we must treat all men as persons.

This last played a great part in his capacity to keep harmony in the staff of which he was the president. We might say that his reign was characterized by harmony in the staff to a greater degree than in any other staff with which I was acquainted. During his reign our staff lived together in mutual harmony and every one had the best opportunity for developing his potential for the common good. He had the great gift of unifying divergent views. Sitting in a staff meeting under his chairmanship was a lesson in wisdom, political astuteness and above all else respect for each man.

Pretense never entered his practice. Inability to help many of our patients evoked humility. Their suffering he attended with compassion. He followed the golden rule as no-one else I know.

It was Marc Antony who said "his life was gentle and the elements so mixed in him that nature might stand up and say to all the world this was a man". How well this applied to Bill Fischer.

Pindar said that "every noble deed dieth if suppressed in silence". His noble deeds will never remain suppressed by silence as long as the Wm. B. Fischer lectureship and the Milford Hospital endure.

Medicine or Magic

But beneath the rationalism and democracy of today's society lurks the same old need for magic, for authority, for someone better or stronger than ourselves to believe in. In medicine it appears in trivial illness and in deadly diseases. You tell a sophisticated patient with a bad cold that there is no cure for it, no relief aside from the drugstore aids he has already purchased. The next day he calls "isn't there something else you can give me for this cold?" As if we had some special remedy that we saved for particularly good patients? And all too familiar is the university graduate with a patient of terminal cancer who insists on a treatment of the latest peculiar concoction from Panama City—"just to give it a chance."

If patients still need magic then they still need magicians—not all the time, not as crude as they used to be but magicians just the same. Here the old tension re-enters the doctor-patient relationship.—*It's hard to be a hero to one's valet and almost as difficult to be an authority figure to friends with whom you have laughed and played.*—Michael J. Halberstram, M.D. in *Medical Thought,* 3: 37, September, 1971.—L.H.N.

The William Fischer Symposium

Host Determinance of Response to Antibiotic Agents

Louis Weinstein, M.D.

What I really want to discuss is not what we are treating, but whom we are treating. I think the emphasis always gets put on the bug and the drug. We see a patient with an infectious disease and our first concern is to try to define the etiology, which means isolating, identifying the organism and then trying to pick a drug that we know, either from past experience or from sensitivity tests, is likely to be the most effective agent and in this concern for these two factors in the infection, we lose complete sight of the third one, and that is the patient. I have been surprised as I have been studying antimicrobial agents and what they do over the years, to find how very frequently we are sort of led away from consideration of whom we are treating, because we get so overwhelmed by trying to solve the problem of what we are treating. So what I want to talk about today is the patient and not either the bug or the drug, and to point out how in essence as one finally looks back over broad experience with this problem, it turns out that the patient is probably the most important determinant of what happens when you treat him for an infection. Now I am not going to discuss the infections that patients have because this is part of the bug and drug problem, but what I want to talk about is how patients influence how you treat them and what happens when you do. One of the factors that is usually and frequently overlooked is the problem of age, and I find that my pediatric colleagues frankly have very little understanding of how dosage needs to be adjusted for children, because I think all of us suffer from the fact that in medical school we learned that you adjust the drug dosage on the basis of kilograms of body weight, or if you are more modern, you do this on the basis of square meters of surface area. Well this applies to many of the drugs that are used and it applies to some of the antibiotics, but unfortunately it does not apply to the antibiotics that are used most extensively, with which none of the rules that we learn in pharmacology have any application at all and the only rules that apply are the level of renal and hepatic function. I would like to discuss first then the problem of age and particularly how it applies to children and how this influences how one picks doses of drugs.

I am going to talk mainly now about drugs that are excreted by the kidney: penicillin, the Cephalosporin derivatives, the colistins, and the mixing group of most of the aminoglycosides, which include streptomycin, kanamycin and gentamicin the most recent one. Most children are born with poor renal tubular excretory function. This is worse in premature babies than it is in full term neonates. It takes about one to two years of life before maximal tubular excretion develops, so that when dose arrangements are made for children in terms of relating this to the adult, you find that you have to make certain adjustments, not on the basis of the child's weight, nor on the square meters of the surface area, but rather on the basis of what his renal function is. It has been shown, for example, that if you take a premature baby, or a group of premature babies, and give them a dose of penicillin, a standard dose, per so much per square meter, and compare this with children that are about 6 to 8-years of age, on the same dose the younger children will have blood levels of penicillin that will persist six times as long as they will on the older child. What this means, of course, is that at one point those blood levels were possibly four to six times higher at maximal serum concentration in the young baby than they were in the older child. It is known also, for example, that if you give a standard dose of 30,000 units of penicillin to a newborn baby, within an hour or so you will have a blood level of somewhere between 80 to 140 units per milliliter, far in excess of what one needs to treat ordinary infections and that you will be able to detect penicillin still circulating at 24-hours. Well, the rule then for the young baby

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is that despite, or because of his small size, but even more important, because his renal tubular excretory function is relatively poor, that you need to make adjustments in his dose downward, but what is lost sight of because again we sort of fall into the trap of correlating this with size rather than with the level of renal function, is we tend to give smaller doses to older children. Once that child gets to be beyond the age of 2, certainly between the ages of 2 and 10 or 12, children require much more penicillin, cephalosporin, colistin, any of the aminoglycosides, any drug that is excreted by the kidney, than do older adults, and the reason for this is again obvious, they are now at the level of maximal tubular excretion. A study we did, for example, about 5 or 6 years ago, we gave children at the age level of 4 to 5, 400,000 units of penicillin in a single intramuscular dose, and did this because our pediatric house officers were sure that this was enough for that child because he was small. Well, the fact was that in 2 hours there was no detectable level. Now children at that age level, anywhere I would say between 3 and 12, who are now excreting maximally need big doses, and we have no hesitancy in giving an 8 or 10 year old child 24 million units of penicillin per day, and at that level he is much safer from the standpoint of developing any of the irritative effects of penicillin than is either an older child or an old adult. Now what I have said so far about the penicillins, I stress, applies to all the cephalosporin derivatives, which includes Keflin, Loridine, probably Cephalexin and Cephaloglycin, and all of the aminoglycosides. The only drug with which one has to be careful in terms of giving a somewhat larger dose, or at least does not have to worry about adjusting dose for size, is colistin and also polymyxin. Both of these agents are excreted by glomerular filtration. Glomerular filtration in the baby is as good as it is in the adult. Therefore the half-life of colistin and polymyxin is not prolonged in a young baby, as a matter of fact the young baby probably excretes it a little better even than the adult, so that on equal doses the maximal serum concentrations in young babies who get colistin or polymyxin will probably be lower than it is in adults.

Well, looking at this in a summary sort of fashion, what I have been trying to say is that you cannot use size, either in kilograms or surface area, to determine what the dose should be of an antibiotic that is excreted by the kidney, and the only determining factor is what the state of renal function is in the baby and that one knows that the baby has poor tubular excretion but that this gets better over the first year. McCrory at Cornell has told me that actually he thinks that it is at age 2½ years before maximal tubular function develops and you adjust your dose on that basis. Well, what happens if you pay no attention to this then, is that the young baby, the very young one, may get over-treated and the older child, the 4, 5 and 6-year old one, gets under-treated, because if one again bases his dose on surface area in this child with maximal renal function you are now giving him a dose that he is going to get rid of in a great hurry, so age is an important determinant in children and adults, and I will make some comments about adults shortly. It is also an important determinant of route of administration. Within the first 24-hours of birth the baby's gastric acidity approaches that of the adult.

Sulfisoxazole, or Gantrisin presents a different problem in the baby. Protein binding of the sulfonamides is with albumin. It just so happens that Gantrisin has a greater avidity for albumin than does bilirubin and so if a newborn child is given Gantrisin there is a tendency now for the Gantrisin to replace the bilirubin that is attached to the albumin, and so these children are now exposed to excessive levels of circulating bilirubin and if this goes on long enough kernicterus is the end result, and this has been very well documented.

The group of drugs that are probably the most toxic in terms of age are the tetracyclines. All sorts of problems have arisen when tetracyclines have been used in young children. As a matter of fact, many people have now suggested that tetracycline should never be given to a child under the age of 12 unless no other antimicrobial agent is available. Well, what are some of these problems?

There is the problem of discoloration, enamel hyperplasia and the fluorescence of the anterior teeth. The ages of 2-months to 2-years represent the period of greatest vulnerability of the teeth because this is the period when the permanent dentition is undergoing calcification. You have to keep in mind also, and pediatricians and obstetricians must be aware of this, that the placenta passes tetracycline with great ease and it gets to the fetus, and if the mother is given tetracycline compound at the right time then the first dentition will be injured. This is aesthetically unpleasant, but usually resolved by loss of the first teeth and so it does not constitute, in terms of the dental problem at least, such a terrible business. The dental injury occurs only when the crowns of the teeth are being formed and this happens from mid-pregnancy to 4 to 6-months of age of the fetus for the deciduous anterior teeth and from 6-months of age to 5-years of age for the permanent anterior teeth.

The tetracyclines are also deposited in bone and when they are deposited there they interrupt bone growth. There have been very good studies in children whose fibulae have been measured and it has been shown that when tetracycline has been given over a relatively short period there is about a 40% depression in bone growth. This is beautifully demonstrated in animals, but has now been well documented in the human child. The longer tetracycline exposure goes on, the less chance there is for bone growth to resume. When the tetracycline has been given for a short period, then despite the fact that there has been this interruption, bone growth will then resume and usually catch up, but if it has gone on long enough then that arrest in bone growth appears to be permanent.

And finally, there is the problem of the so-called pseudotumor cerebri with the tetracycline compounds which is commonest in children but also occurs in adults, and we have recently seen an adult with pseudotumor cerebri from a tetracycline compound. This is not related to the dose, or duration of therapy, and it seems to be a problem associated with the use of any of the tetracycline compounds.

So then, when you look at age now, in terms of children, what you do really see?

(1) That age determines dose of most of the commonly used antimicrobial agents.

(2) Age is an important determinant now of the route of administration.

(3) Finally, in the child especially, based purely on the functionally biochemically disturbed child, which is normal for him, age is an important determinant of some very significant types of untoward effects.

Well, is this a problem only in children? No, it is a problem also in the adult, and especially in the older adult. Unfortunately, as we age so do our kidneys, and the presence of normal renal function, as demonstrated by the conventional tests, the BUN, serum creatinine, or even creatinine clearance, does not indicate what the problems may be when one gives an antibiotic that is excreted primarily by the kidney. I think that one can assume, if you will accept a fairly broad experience to back this up, that after the age of 50 none of us have completely normal renal function, and you have to be careful how you give drugs that are excreted by the kidney. We have data to show, for example, that if you take a group of people between the ages of 60 and 70 and give them 100,000 units of penicillin intramuscularly, 12 to 18-hours later you can still demonstrate penicillin circulating in the blood. If you do this to a 10-year-old child you probably would not be able to show anything at one hour and certainly not at two hours. So that any drug that needs to be given that is excreted by the kidney, needs to have a reduction in dose when you get into the older patient and I will have some comments specifically about the problems of renal function a little bit later, but just let me point out an experience that I think underscores what this problem is. For many years we gave all adults 5 milligrams per kilogram of colistimethate (colistin), but we found, however, that in doing this a large number of these people, having started with normal BUN's and creatinines, now developed varying degrees of azotemia. We therefore began to reduce the dose and we find now that a better dose, even though it is not the recommended or conventional dose, a dose that is very apt to spare this injury to the kidney, is 3 milligrams per kilogram, and even with this we occasionally will produce elevation of both the BUN and serum creatinine levels. You can take advantage also in the older age group of the fact that about 60% of people over the age of 60 have a varying degree of achlorhydria; they may actually be totally acid free or they are secreting small quantities of acid so their gastric juices or pH is well above 2½. We also know from experience that we can give older people a dose of penicillin by mouth and get perfectly good levels and a fairly good therapeutic effect in some of the less involved types of disease, when that same dose given to somebody in his second or third decade of life, given by mouth, will produce very poor levels and have very little affect on an infection. So this problem of age now determines not only management of antibiotics in children, but also plays an important role in adults. There are a number of other factors, but I have limited time and I have picked out 9 others to discuss briefly.

The problem of genetic factors. We have a large stable of patients with ulcerative colitis, some 200 now, whom our gastroenterologic group is studying medically, psychologically and every other way, and one of the drugs they use is Azulfidine, paying no attention to the possibilities of Azulfidine producing reactions since it is not absorbed by skin and by mouth, and they first began to give it without much consideration to the patient, they were interested in the disease and the drug, until all of a sudden one of their patients developed a severe acute hemolytic anemia. It is then that they first began to worry about the problem of glucose 6-phosphate d-hydrogenase deficiency, (g.6 p.d. defect), and now this is done routinely before anybody is put on Azulfidine and it turns out that between 1 and 2% of our white patients, and 1% of the black males and about 10% of the black females, have the g-6 p.d. defect and you cannot give them Azulfidine without running risks of producing severe hemolytic anemia. Now what is also very intersting, is that although the incidence of this defect is lower in the white than it is in the black, when it is provoked by the administration of a drug the hemolysis that occurs is usually more severe in the white man than it is in the black patient. So one needs to be careful in giving certain drugs to make sure that this patient does not have this enzyme defect, else you are apt to produce a severe hemolytic anemia. Now what are the drugs? Well, they are some of the commonly used ones: Sulfacetamide which ophthamologists like to use a lot. Two drugs that were used a lot but fortunately have been dropped, Kynex and Madribon. I have mentioned Azulfidine. Gantrisin—as little as four grams of gantrisin has been responsible for an acute hemolytic anemia. Furadantin (nitrofurantoin)—patients described who have taken 600 milligrams, that is a-day-and-a-half of treatment, and have gotten into trouble with acute hemolytic anemia. And finally one of the drugs that is used in leprosy gatsa which has also been responsible for provoking the activity of this enzyme defect. Those of you who use Isoniazid also have to keep in mind that there are genetic factors that influence dosage. The American population is divided into two groups, the rapid inactivators and the slow inactivators. McKusick at Hopkins published a very nice review of this problem in "Lancet" 5 or 6 years ago, and showed that there are certain ethnic differences in the distribution of rapid and slow inactivation. What we are dealing with mainly in this country is the white population where he and others have shown that this distribution is probably about 50-50. The question then is, of what importance is this, and what does it do? I surmise that again it is biologically inactivated in the liver by combination with acetyline, the acetilated Isoniazid is the biologically inactive form, and this difference in rate of inactivation has to do primarily with how much acetyline gets attached. Thus, two questions come up. What happens if you give a rapid inactivator the standard dose and secondly, what happens if you give the slow activator the standard dose? There is not very good evidence that the rapid inactivator will get into any difficulty therapeutically if you give him the standard dose. There is one report in which it is claimed that the therapeutic effect was not so good in a group of patients who were found to be rapid inactivators of Isoniazid, but there is clear-cut evidence that the slow inactivator may in fact get into very serious trouble. He has good and bad effects from this. Because he is a slow inactivator he has circulating for longer periods and at higher levels biologically active Isoniazid, so he gets more for his "dough," but at the same time exposure to these high levels exposes him to a greater risk of toxic effects. I have one patient who I think showed this beautifully. He was a neurologist who worked in our hospital, who developed renal tuberculosis. Not wanting anyone in the hospital to know about this he went outside for his medical care and was treated with Isoniazid at a dose of 300 mgs. a day and some para-aminosalicylic acid. He got along well for a couple of weeks and then a couple of weeks later I was asked to see him because this fellow was just, as you might say, "out of it." He had developed terribly bizarre mental symptoms, he had jerkings and neurological problems. What had finally disturbed his family was that he had taken off one day for the hospital and wound up in Portland, Maine, not knowing that he was even going there. The more we talked to him and his wife, it became apparent that his reactions were extremely bizarre and the question was raised whether he was not having Isoniazid toxicity. We did some studies with him and found out that he in fact was a very slow inactivator of Isoniazid, he generated very high levels on a relatively small dose. We got him down to 100 mgs. of Isoniazid once a day. His tuberculosis, as far as we knew, was getting along all right and within about a week all of his neurological and mental symptoms cleared. So there certainly seems to be evidence that a genetic factor, particularly one that influences slow inactivation of Isoniazid may play an important role in determining toxic effects to this agent.

Now let us look at a third factor—pregnancy. There are a lot of problems in giving antimicrobial agents to pregnant women. In the first place you are not dealing with one patient. Many of the antimicrobial agents pass the placenta, and so you have to consider the questions as to what you are doing to the pregnant woman and what also may you be doing to the fetus? There are some data, unfortunately not enough, as to what goes on in terms of placental transmission of antimicrobial agents, but we have learned, again from clinical experience, what some of the problems may be. For example there is very good evidence that pregnant women probably should not get streptomycin, except for very short periods, because there are now two very good studies that have clearly pointed out that the babies born to mothers who have had relatively small doses of streptomycin but over a long period, have had either vestibular dysfunction which is the commonest defect produced by streptomycin itself, or when somewhat larger doses have been given for somewhat longer periods, those babies have been deaf. So that certainly, in a pregnant woman, even with normal renal function, streptomycin should be avoided. The biggest culprit because it probably is, or at least was for a time, a very widely used group of drugs, are the tetracyclines. Tetracyclines harm the pregnant woman by doing a job first on her kidneys and then on her liver. Now unfortunately, tetracyclines have been used most often during pregnancy for the treatment of urinary tract infections and usually for involvement of the upper part of the urinary tract. There is good evidence, for example, that if you give a normal person the conventional dose of tetracycline, which may be let us say up to 2 grams a day, if he has a normal renal function nothing will happen, but if you give a patient who has somewhat decreased renal function that dose of tetracycline, his BUN and creatinine, which have already been elevated, will become even more elevated. While there is no good evidence that tetracycline injures the perfectly normal kidney, there is good evidence that it will produce additional injury to a kidney that has already been injured by something else. So that is one facet of the problem.

The other, in terms of the pregnant woman, is based on studies particularly late in pregnancy, that show that many women will have, for example, abnormal BSP's. There is some evidence that there is a degree of hepatic dysfunction late in pregnancy. Biopsy studies have actually shown collections of fat in the liver late in pregnancy. So that even in the perfectly normal pregnancy one needs to consider when giving any drug that is going to be handled in the liver, the possibility that there is already established some degree of anatomical liver damage in terms of fat infiltration and functional disorders as demonstrated by elevated BSP, or retention of BSP.

Now you take these two facets, and add to this the fact that all tetracyclines are handled both in the liver and in the kidney, they just vary in the degree in which they are handled in each of these organs. For example, chloretetracycline, which is Aureomycin, is handled much more in the liver than it is in the kidney, whereas tetracycline itself, or Declomycin, is handled much more in the kidney than in the liver, but the fact that I stress is that both of these organs are involved in both the metabolism and the excretion of the tetracyclines.

Now if you put this together, with the problems in the kidney and the liver in the pregnant woman who has pyelonephritis, you should not be surprised that there have been two papers within the last 10 years, both in the New England "Journal of Medicine," reporting death in women from combined hepatic and renal failure when they had been given conventional doses of tetracycline compounds by mouth (the conventional dose, as I have pointed out, is up to 2-grams.) That the tetracyclines do things to livers that are already injured we learned for ourselves. Some years ago we worked in one of the state schools, Remkin State Hospital, doing various studies, and in that hospital almost every year they have an epidemic of viral hepatitis and this is common in the mental disease hospitals throughout Massachusetts. We went out there several years ago and picked out a group of children, about 10, who had been involved in a viral hepatitis epidemic some 6 or 7 months before. My fellows and I studied their liver function by doing transaminase levels, alk.phosphatase, BSP excretion, and all of their functions were normal. We then gave them one gram of tetracycline and went back at the end of 2 days, 7 days, 10 days and 2 weeks and re-studied their transaminase levels and their alk.phosphatase. Within 48-hours every one of these children had elevated transaminases, had elevated alk.phosphatase and had developed BSP retention. This lasted for about 10 days and then disappeared. We did not repeat this study and we have not yet published it. I think this kind of study needs to be done over before we are sure of our results, but what we are trying to prove to ourselves is that the patient who has viral hepatitis really does not have a normal liver despite the fact that all his enzyme tests are normal, and that in the presence of clinically inapparent dysfunction, or dysfunction not apparent even by rather elegant biochemical tests, one can still demonstrate by provocation the presence of active disease, that is active at a very low level, by giving a drug that is known to require the functioning liver to conjugate it and it is also known to injure the liver. What I have said about the tetracyclines so far certainly suggests that they should not be used that extensively. As a matter of fact, just to sum up, one pediatrician who has written about this has almost pointed out that tetracycline compounds certainly should be used nowhere in pediatrics, they should be avoided like the plague in pregnant women, and given only if there is no other available antimicrobial agent, and that is not a problem today.

Let us now look at another facet, metabolic abnormalities. We ran into this as a problem several years ago. I had a patient with subacute bacterial endocarditis with a very sensitive strep viridans in whom we demonstrated the sensitivity in an organism, we did blood levels we thought were worthwhile, we treated him with what we thought was an adequate dose but he failed to respond. As we continued to do blood levels we were rather surprised that his maximal serum concentrations were not what we thought they should be, so all we did was to increase the dose until he finally responded, was cured and went home. A few months later we got another one that did exactly the same thing. Again we just increased the dose, he recovered and he went home. But this plagued me, and a few months later I dragged out both records and studied them and found much to my surprise that they were the first two patients with diabetes that I had ever taken care of who had subacute bacterial endocarditis at the same time, which started a study which then took 3-years, the summary of which I can tell you in about 2 sentences.

Diabetics absorb penicillin from intramuscular sites very poorly, they do-not do this in the same manner as do the non-diabetics. We went through a lot of machinations trying to find out what the mechanism for these relatively low blood levels were, including studies of half-life destruction. It turned out that this is all due to absorption, because as we studied the two phases that occur in the absorption, that is the up-take in terms of the development towards maximal serum concentration and the down-stroke as the patient was losing penicillin from the blood. We found that the down-stroke in these patients when compared to the down part of the curve in a group of controls of the same age and sex were identical. In other words, the half-life of the drug was the same in the diabetic and the non-diabetic, but it was the up-stroke that was different, because in the first place the slope was shallower, in other words the penicillin was getting into the blood at a slower rate, and the maximal serum concentration in the diabetics was always much lower than it was in the non-diabetic, again pointing out clearly the fact that penicillin was being absorbed poorly from intramuscular sites in the diabetic. At first, we thought is it peculiar to only penicillin, so we went to sulfonamides and it turned out that it was exactly the same with sulfonamides. We then did muscle biopsies, thinking that we could relate this to the so-called small blood vessel disease that Siprus found in Texas and has made claims for in terms of this being the basic lesion of diabetes mellitus. We could make no such correlation, but that it had somthing to do with age we found when we studied this in children. Diabetic children do-not exhibit this phenomenon, they pick up penicillin from intramuscular sites just as well as do non-diabetic children. While we were doing this work Chalmers at the Shattuck Hospital in Boston, did some studies with insulin and it may surprise you to learn that diabetics do-not absorb insulin very well from intramuscular or subcutaneous sites and this again may be due to some type of blood vessel problem with which we are not acquainted at all. There are also other metabolic abnormalities which I do-not have the time to discuss, so let me skip to the next one.

No-one should ever give a patient an antimicrobial agent, particularly one of the penicillin derivatives without asking about his general history regarding a lot of atopies; is he sensitive to ragweed, roses and to dust? If he is, you had better be extremely cautious as to how you give him penicillin. There is a very distinct correlation between a deep history of various types of the atopic allergies and a risk of reaction to antimicrobial agents, especially to the penicillins.

Now, let us look at another host factor, the nervous system. How does this influence what kind of drugs and what doses we give? Everybody knows about the fact that the aminoglycosides; streptomycin, kanamycin, neomycin, and the colistin polymyxin group, may produce respiratory paralysis when given to patients. This was first noted when patients had neomycin pumped into their bellies after an operation and had immediate shut-off of respiration, and especially in patients who were getting succinylcholine as a relaxant. Well, what has been found, or suggested, is that the aminoglycoside antibiotics have a curare-like effect and so they tend to potentiate any other agent that has a curare-like effect at the myoneural junction and this is frequently reversible merely by the administration of physostigmine. Multiple sclerosis patients should never be given aminoglycosides—no gentamicin, streptomycin, kanamycin, because again paralysis of the myoneural junction in them may turn out to be a fatal event as they are already in serious difficulty, sometimes just barely able to support their respiration and if they suffer this curare-like effect of the aminoglycosides in addition to the difficulty they already have, this may spell doom. Then there is another interesting set of reactions that have to do with penicillin on the central nervous system and this brings in some very interesting physiological principles. Some years ago I got interested in treating gram negative bacterial infections with what I like to call "massive doses of penicillin". They sound massive when you start talking about 60 and 80 million units of penicillin. I think that term "million" is what bothers everybody, if I said 60 days of mega nobody would worry about it very much. The fact is that many people around the world are now using these large doses because they have been found to be very effective in treating not only some gram negative bacterial infections, but also some gram positives, but there are problems with these large doses and they have to do primarily with affects on the central nervous system. Nobody knew the effects of penicillin on the central nervous system until Fischman at Columbia did some very beautiful studies and showed that the cerebral spinal fluid blood barrier for penicillin was constituted of two membrane pumps which are in the choroid. One pump pumps penicillin into the spinal fluid and this is a non-energy requiring system. The other pumps penicillin out of the system, is not dependent on the blood level of penicillin but requires energy. In other words, uncoupling of oxidative phosphorylation has to take place, ATP-ase is involved to make this pump go. What Fischman found, and we later confirmed in a small study that we did, was that this pump that takes penicillin out has a capacity can be exceeded and it is exceeded when you give penicillin by constant drip, particularly if you give it in large amounts. We did a study on one "volunteer" (this is an out-patient, usually a dental student and for $100 they let us do things.) We gave him 50 million units of penicillen intravenously in a rather rapid run, in over about an hour he got the 50 million units. We had a platinum needle in his spinal canal because it can be bent over and you can keep it in and take out spinal fluid when you want it. We studied his blood and spinal fluid levels and he developed a fair level in his spinal fluid, but what we felt was below the epileptogenic concentration. He had no clinical manifestations and we followed his blood and everything was "hunky dorey." We had contracted with him to come back a few weeks later for another $100 and this time we were going to give him the 50 million units in a slow drip, which we did. And as we followed this (we learned this later), as we dripped in the stuff after about an hour-and-a-half he began to twitch and at that point we stopped, we did not want dental students having seizures on our service. We then found as we studied his blood and spinal fluid levels that although he maintained a fairly constant blood level, his spinal fluid level began to climb out of proportion to his blood level, which was just confirming what Fischman had said. In other words, what we had demonstrated for ourselves was that we had exceeded the capacity of the pump to take penicillin out of the spinal fluid. Now what are the factors that you have to be careful of?

(1) Do-not give big doses of penicillin to people with renal failure because they cannot excrete it.

(2) Any patient who has either localized of diffuse cerebral disease should not get massive doses of pencillin, because if it is localized they will have a Jacksonian fit and if it is diffuse they will have a typical tonoclonic epileptic seizure.

(3) The third point we learned in our study of these large doses, particularly in relation to the nervous system, was that for reasons unknown to us and to anybody else, although this observation has recently been confirmed, patients whose plasma sodium levels are low seem to be much more predisposed to seizure than those who have a normal sodium level.

Since we were using potassium penicillin we think this may be playing some role in the exchange of water in the cerebral cells, but we are not at all certain and I do not want to bore you with speculations. The observation that we think is accurate is that if the plasma sodium is low you have got to get it up to a normal level before you go ahead and give large doses of penicillin. Well I am going to skip one because time is getting short.

Let me get the problems of hepatic and renal function, and again I am not going to bore you with a lot of detailed information which is available in literature to point this out, except to try to tell you two rules that I have found extremely helpful, and this, incidentally, points out very sharply that physicians who use any drug should be aware of the pharmacology of the drug and since I am talking about any microbial agent, it seems to me that you are exposing patients to great risks if the physician at least does not know how the drug is absorbed, excreted and metabolized, and everybody should know which antibiotics are handled in the liver, and which are handled in the kidney, because if you do-not know this patients are very apt to get into trouble and the rules are very simple. If you have somebody with decreased liver function do-not give him a drug that has to be inactivated in the liver because he cannot do it, or if he does it, he does it inadequately, and therefore is exposed again to circulating excessive concentrations of drug which may be poisonous. This is beautifully brought out by the late Dr. Orson Wiseberger. He took a group of cirrhotics, all of whom obviously had rather severe liver disease and he gave them conventional doses of chloromycetin. I have already pointed out that chloramphenicol needs to be conjugated in the liver. These people could not conjugate it well, so that although chloraphenicol produces anemia in everybody who takes it, what Wiseberger found out was that the anemia developed exceedingly rapidly and the levels of hemoglobin were much lower than in controls of the same age with normal liver function. I do-not think you need any more proof for this. So the rule . . . Do-not give drugs that are conjugated in the liver to people with decreased liver function. Some of these drugs are Isoniazid, erythromycin, novobiocin, all of which are among the fairly commonly used agents. There is another problem with the liver. Some drugs are concentrated in the liver, and there is an argument as to whether they are actually concentrated or just held back in the liver and the best example of this is Ampicillin or Polycillin, I guess it is called. Ampicillin is held in the liver so that it gradually accumulates and if you study gallbladder bile levels and compare them with blood levels the levels in the bile will average about 30 times higher than in the blood, but there are studies now showing that if you take a patient with decreased liver function and give him the same dose of Ampicillin, he now does not develop those high concentrations of Ampicillin in his bile. We use Ampicillin very often to treat infections of the liver. For example, this is proved to us to be one of our best agents for management of acute exacerbation of chronic cholangitis, or to treat, not always successfully, multiple liver abscesses, but if the patient's liver function is poor then the patient does not have the advantage now of retention of drug in his liver so that he does not get the maximal effect.

What about renal function? I think I have already suggested enough points about this to make what I am going to say in a moment somewhat redundant. The rule is simple . . . know what drugs are excreted by the kidney. Do-not give them to patients with decreased renal function if you can avoid it. We have already discussed many of the drugs that are excreted by the kidney. There are instances in which it becomes absolutely necessary to give a drug excreted by the kidney because that is the only drug that will control the infection. What do you do? A mistake that has been made up to now is to reduce the dose. That is absolutely the wrong thing to do, because there is no problem with absorption in the people with decreased renal function, they will pick up the drug. If you give them a small dose they now wind up with a level in the blood and tissue fluids which may be ineffective in terms of attempting to eradicate the organism. Give them the standard dose. If you were going to give a patient 24 million units of penicillin a day, or 2 million units every 2 hours, and he has no renal function, you give him 2 million units of penicillin, but what you do now is to lengthen the interval. He may not need any more penicillin for the next 12 to 24 hours, or he may need some within 8 hours. There is a fair amount of data in the literature concerning this whole problem of dosage and interval for most of the commonly used antibiotics. I do-not carry this around in my head, but just as an example, it is now suggested that if a patient has a BUN of over 150, if you give him Gentamicin you give him a standard dose, but you do-not give him the next one until 24 and sometimes 48 hours later. So the rule is to be careful of the drugs that are excreted by the kidney in the patients with renal failure. When you need to treat give as a single dose the dose that you would give if renal failure was not present, but now be careful of the interval at which you give the doses. Unfortunately, many of the agents that are excreted by the kidney are also nephrotoxic, and this is certainly true of Gentamicin and the other aminoglycosides. So there is double trouble and certainly much need for real caution in the way people are given these drugs when their kidneys are not functioning normally. Now there is one thing about penicillin that I do-not think many people know that I would like to bring to your attention. 10% of penicillin is filtered by the glomerulae and 90% is excreted by the tubules. In patients with total anuria, in other words the patient who has no renal function at all, who is putting it out only via his sweat, you can give him penicillin because in this instance the penicillin would be degraded in the liver and about 7 to 10% of a dose is degraded in the liver per hour. So we give penicillin to people with decreased renal function, figuring that about 7% will be lost in the liver per hour, so if we give say 10 million units and we figure out 7% of 10 million units we now can calculate the interval roughly at which we will give the next dose. What are the agents that are safe in the patients with renal disease? Those that are handled in the liver, and so we had given some of Dr. William Schwartz's patients with acute tubular necrosis who had not put out a drop of urine for 3 weeks, 4 grams of chloramphenicol intravenously, per day, with no problems at all. They just biologically inactivate it, this circulates, it is non-toxic, and this is gone on until the patient's renal function has returned and everything has been as they say, "hunky dorey."

Now let me get to the final and the most critical factor that really determines whether patients get better or not when you give them antibiotics. So far I have been talking about how all these things determine dose, type of administration, etc., and now I want to talk a little bit about what really determines whether a patient is cured or not, and I am going to make a statement that in some circles sounds heretical, but I am a heretic. I am thoroughly convinced that no antibiotic ever cured an infection by itself and I have plenty of clinical data to prove this. In other words, what I am trying to say is that all the antibiotic does is to prepare the organism for its eradication by the normal defense mechanisms, that is all, and you see this if you happen to work in a hospital where a lot of hemologic problems, patients with no white cells, no gamma globulin, or none of either, who are smashed up by their disease in terms of being badly immuno-suppressed, who are then given various cytotoxic agents which are even more immunosuppressive. Then you find a patient with pneumococcal pneumonia and bacteremia who fails to respond to penicillin and dies, or as we have seen one patient (and this was a fantastic example of just what I am talking about)--a lady who was known to us for some years with systemic lupus, who while far out in the country, away from Boston, developed a belly-ache, (she had been getting a course of steroids) had a very smart doctor who despite the fact that there was only little tenderness in the belly made a diagnosis of peritonitis, she was operated on, she had pneumococcal peritonitis. He treated her with large doses of penicillin and increased the corticosteroids because of what he thought was an increased stress reaction, and then 5 days later she was sent to our hospital with pneumococcal meningitis; this despite the high level of sensitivity of her organism and she was getting massive doses of antibiotics. We treated her, we thought rather intensely, she lived longer than we expected, she lived a week, and at the end of that time when she came to autopsy and I made smears of the exudate of the face and the brain I still saw pneumococci which I was unable to culture. Every year we see half-a-dozen, at least, of such cases infected by organisms that are sensitive, that are not always penicillin sensitive, but they are at least susceptible to some agent. These patients are treated intensively, but they are immunosuppressed by disease and this immunosuppression is made even deeper by the drugs they are getting, and they die despite, what should have been, effective therapy. This is what has convinced me over the years and I think I am beginning to collect some disciples of the fact that we do-not cure patients with antibiotic agents, they cure themselves. What we do with the antibiotics is to just make it possible for the patient to cure himself. Which brings me to my final point, and this always racks up people, particularly my colleagues in Boston.

I do-not think there is any proof that a drug which is bacteriocidle in vitro is bacteriocidle in vivo, because we have patients dying from infections due to organisms treated with drugs that are bacteriocidle in vivo. As a matter of fact, if you want proof of the importance of the intervention of adequate host defenses, you just need to look to what happens when you give a patient a bacteriostatic drug. By definition the sulfonamides, the tetracyclines, chloramphenicol, are bacteriostatic drugs which means that by interrupting protein synthesis they just sort of stop the organism, it does not multiply but it is not dead. As a matter of fact even Streptomycin has been shown not to kill organisms just in the way that it used to be thought it did. Well, if that is the case then, the patient should remain well while we are giving him a bacteriostatic antibiotic, but soon after the drug is stopped the patient should relapse, but they do-not. In other words, we are curing infections with bacteriostatic drugs, which again must mean, at least to me, that what we are seeing operating here is effective defense mechanism.

Well, just to summarize quickly what I have attempted to do is to point out the importance of the patient, because I think that as one thinks about the management of infection and the results of exposure to antimicrobial agent, it turns out that the patient is actually the most important determinant in what happens when he is treated for infection, forgetting the infectious process itself. I do-not deny, and as a matter of fact I am a very strong advocate of, the necessity to determine sensitivity of organisms, to know about blood levels, the antibacterial activity of serum in the management in following the progression, or the course of the disease. These are all terribly important pieces of information one needs to have to manage infections properly, but I think what we have done over the years is with our attention sharply focused on the problem of the bug and the drug, there has been a great tendency to overlook the patient, and what I have been crusading for over the last couple of years as I have become more and more interested in this problem of the host, is that our concern be not only for what we are treating, but if we want to produce the maximal effectiveness of therapy with the least risk of harm to the patient, then we have to give important consideration to whom we are treating.

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Urinary Tract Infections

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Except for infections of the upper respiratory tract, urinary tract infections represent the most common type of infection encountered in the practice of medicine. The magnitude of this problem has been responsible for intense investigation of urinary tract infections in an attempt to better understand the etiology, pathogenesis, natural history and treatment of this disease. Although effective therapy for most bacterial infections has been developed since the advent of antimicrobial agents, considerable controversy still exists over the proper approach to the treatment of urinary tract infections. The purpose, therefore, of this report is to describe our approach to the treatment of these infections.

A urinary tract infection is defined as infection caused by bacteria and situated between the external urethra and the kidneys. The diagnosis of urinary tract infection is currently based on the demonstration by culture, of the presence of a significant number of bacteria per milliliter of urine. The number of bacteria recovered from the urine is important because although bladder urine is normally sterile since bacteria are not filtered from blood into urine by the kidney, the presence of any number of bacteria in bladder urine would constitute an abnormal finding, unless the bacteria contaminated the urine during collection of the sample being cultured. Guidelines for the separation of contamination from infection became available with the introduction of quantitative bacteriology into urine cultures. This technique obviated the old practice of obtaining urine cultures by bladder catheterization. The latter procedure in itself, subjects the patient to the risk of acquiring urinary tract infection from the instrumentation since bacteria may be introduced into the bladder during passage of the catheter through the uretha.

By using the technique of quantitative bacteriology, true bacteriuria (urinary tract infection) can be distinguished from bacteria introduced as contaminants. The rationale for this is based on the observations that bacteria originating in the kidney or bladder multiply quickly in the urine at body temperature in numbers usually greater than 100,000 colonies per milliliter of urine, whereas urine contaminated during collection usually contains less than 10,000 bacterial colonies per milliliter of urine. Consequently, in the majority of patients, quantitative culture of a clean voided midstream urine sample is adequate for proper bacteriologic diagnosis.

Urine specimens for culture can be obtained by the clean midstream voiding technique which is essentially the same for both sexes. The vulvar area or penis is cleansed by two applications of tincture of green soap (benzalkonium solutions are not used since they may become contaminated with gram-negative organisms) followed by two rinses of sterile distilled water. The patient starts to void (in women, the labia should be held apart), allows the first portion of the stream to be discarded, and collects the midstream urine in a sterile container. The collected sample should be cultured within 30 minutes or refrigerated promptly until it can be cultured since urine is an excellent medium at room temperature and will support the multiplication of gram-negative organisms which will result in a spuriously high bacterial count. If the urine can not be cultured immediately it can be refrigerated for periods of at least one week without a significant change in the number of bacteria.

There are a variety of methods to quantitate the bacterial count in the urine. One rapid screening procedure is to examine a drop of uncentrifuged urine with the high dry lens of a microscope. The presence of a few rods in the urine strongly suggests a colony count of at least 100,000 bacteria per milliliter. However, this procedure does not exclude the possibility that there are 100,000 bacteria per milliliter of urine whenever bacteria are not seen in the uncentrifuged drop of urine. In addition to the screening procedure, the urine should be quantitatively cultured.

A rapid inexpensive method of quantitating the bacterial count in the urine involves the use of a standardized calibrated inoculating loop which is used to streak a loopful of uncentrifuged urine onto a solid agar plate. After 24 hours of incubation, the concentration of bacteria in the urine can be calculated by multiplying the number of colonies on the plate by the appropriate dilution of urine

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contained in the calibrated loop. For example, if the loop is calibrated to carry 0.001 milliliters of urine, the number of colonies counted on the plate, multiplied by one thousand would equal the number of colony forming bacterial units per milliliter of urine.

A second simple procedure, the stroke-plate method, also requires a calibrated inoculating loop which delivers a known volume of uncentrifuged urine onto a blood agar and an eosin-methylene blue (EMB) agar plate. (The EMB plate will only support the growth of gram-negative organisms.) The loopful of urine is plated across one edge of the plate using approximately 20 strokes over a width of about one cm. With a second sterile loop an area one cm. wide is plated at one end and at right angles to the original inoculation. This procedure is repeated twice to produce a square on the plate with each side one cm. thick. After 24 hours of incubation growth is noted as one, two, three or four plus depending on whether one, two, three or four sides of the inoculated area show colonies. Approximately 85% of urines with three or four plus growth will contain 100,000 or more organisms per milliliter of urine.

A third method, which is the most precise and is used in our laboratory, but is time consuming, consists of preparing an agar pour plate of a one to one-thousand dilution of urine. One-tenth of a milliliter of uncentrifuged urine is added to 9.9 ml. of sterile saline and mixed. A volume of 0.1 ml. of this dilution is then added to a tube of melted agar, thoroughly mixed and poured into a sterile petri dish where it is allowed to harden. After 24 hours of incubation, the number of colonies are counted by means of a transillumination device. The number of bacteria per ml. of urine is calculated by multiplying the number of colonies visible on the agar plate by one thousand.

The use of quantitative methods gives much more positive guidance as to the presence or absence of infection. If the bacterial count is over 100,000 organisms per ml. of urine in a properly collected and cultured urine, infection is present, if it is below 10,000 organisms per ml. infection is absent. When the bacterial count is intermediate, between 10,000 and 100,000 organisms per ml., infection should be suspected and a second and occasionally a third urine sample should be studied. Two or three consecutive and properly collected urine cultures with an intermediate bacterial count but showing the same organism with the same antibiotic sensitivities suggest the abnormal presence of bacteria in the bladder urine.

Acute Urinary Tract Infections

Usually these patients are women and they present with symptoms referable to either the lower tract (dysuria, frequency, burning, dribbling, suprapubic tenderness) or upper tract (flank pain, chills and fever). Almost all of these infections are caused by *Escherichia coli* or *Proteus mirabilis.* We have found sulfonamides to be the most valuable agents in these patients because of their effectiveness, low cost and lack of side effects. The type of sulfonamide used seems to make little difference. Although we prefer the more soluble sulfisoxazole, equally good results can be obtained with other sulfonamide preparations. An initial dose of 2 grams of sulfisoxozole is followed by a dose of 1 gram every 6 to 8 hours for 10 to 14 days. There is no good evidence that longer courses of treatment are more successful in this group of patients than 10-14 days of therapy. Fluid intake should be increased to ensure a high urine output. Sulfonamides are also effective in the treatment of bacteriuria in pregnancy. Because of the claim that sulfonamide therapy can contribute to neonatal hyperbilirubinemia, they should not be used late in pregnancy particularly during the last two weeks.

Ampicillin (0.5 gm. orally every 6 hours), nitrofurantoin (100 mg. orally three or four times daily), and the tetracyclines (250 mg. orally every 6 hours) are alternative choices for the treatment of acute infections but have not been shown to produce a higher cure rate than sulfonamides, and they are more expensive. An essential part of the care of patients with urinary tract infections is the follow-up which is often neglected because virtually all patients become asymptomatic even without treatment, yet bacteriuria will persist. In the absence of an obstructive lesion, the urine should become sterile within 48 hours after treatment is begun if the organism is sensitive to the agent used. Even following chemotherapy, recurrences occur in approximately 20 per cent. Follow-up urine culture is the only way one can detect that group of patients with recurrent infection or those who fail to respond to the initial course of therapy. We re-examine the patient two weeks after therapy is stopped. If the patient's urine control is sterile at this time, repeat urine cultures are obtained at monthly intervals for 3 months. The patient is considered cured of her infection if the urine culture remains sterile during this follow-up period.

A number of patients will not be cured. They either fail to respond to the initial course of therapy or have recurrence of their infection usually within the three month interval. In some, the recurrence is a relapse of the initial infection with persistence of the original pathogen. In others the recurrent infection is caused by a new organism and is termed a reinfection. Treatment of those patients who fail to respond to an initial course of sulfonamide should be with a different oral agent since a further course of a sulfonamide produces a poor cure rate. We use ampicillin or nitrofurantoin in the dose outlined above for 10 to 14 days for failures of primary treatment. Those patients who experience a second relapse are then given a urologic investigation to determine whether obstructive disease is a factor in the recurrence. This includes an intravenous pyelogram, cystoscopy and voiding cystourethrogram. Retrograde pylegraphy is rarely needed unless there is evidence of ureteral obstruction. It should be emphasized that whenever men, particularly in the younger age group, present with urinary tract infections which are not due to prostatitis, they are immediately scheduled for urologic investigation.

Asymptomatic Bacteriuria

Patients with asymptomatic bacteriuria of unknown duration constitute the largest group of patients with urinary tract infection. Their bacteriuria is usually found during the course of examination for other complaints. This type of patient is all too frequently overtreated because the diagnosis of asymptomatic bacteriuria is not clearly established before the physician decides to start therapy. The diagnosis should be based on at least two and preferably three, accurately collected and properly cultured urines which show the same organism in significant numbers with the same antibiotic sensitivity pattern. Therapy can easily be withheld until the diagnosis is properly established since the patient is asymptomatic. Although *Escherichia coli* is the predominant organism in this group of patients, infections may also be caused by Enterobacter, Klebsiella, Proteus and occasionally Pseudomonas species. Treatment in this group of patients is therefore based on the antibiotic sensitivity of the organism isolated from the urine culture. We prefer to treat them with oral antibiotics such as the sulfonamides, ampicillin, nitrofurantoin, tetracyclines, or methenamine mandelate combined with methionine whenever possible.

The asymptomatic bacteriuric patient requires the same follow-up procedure as outlined for those patients with acute infections, after therapy is completed. Unfortunately, the reappearance of significant bacteriuria after treatment is considerably greater in patients with asymptomatic bacteriuria as compared with those patients with acute urinary tract infections. Patients with asymptomatic bacteriuria who experience two recurrences are subjected to urologic investigation in the manner previously outlined.

Chronic Bacteriuria

Chronic bacteriuria may arise in different ways. Patients with acute infections may go on to develop asymptomatic bacteriuria which may then become chronic. Over the course of a few years some patients may have symptomatic flare-up of their bacteriuria while others may have repeated episodes of acute infections but are asymptomatic and abacteriuric between these attacks. All patients with chronic bacteriuria should be subjected to urologic investigation. The treatment of chronic bacteriuria remains controversial. The organisms most often encountered in these patients are species of Enterobacter, Klebsiella, Pseudomonas, indole-positive Proteus as well as *Proteus mirabilis, streptococcus faecalis* (enterococcus), and antibiotic resistant strains of *Escherichia coli.* Consequently the optimum choice of therapy is based on antibiotic sensitivity testing of the organism isolated from the urine. Again we use oral agents whenever possible. The sulfonamides and chloramphenicol have not proved to be as effective as ampicillin, nitrofurantoin, the tetracyclines and nalidixic acid in this group of patients. Certain refractory cases may require hospitalization for a course of parenteral therapy. The choice of drug will again depend upon the sensitivity of the organism. Some success has been achieved in these patients with intramuscular administration every 8 hours of kanamycin in a dose of 5 mg. per kg. or gentamicin in a dose of 1 mg. per kg., as well as polymyxin (1.25 mg/kg) or colymycin (2.5 mg/kg) every 12 hours. Carbenicillin, a new semisynthetic penicillin which must be given parenterally, is not yet commercially available but has significant activity against most strains of Pseudomonas and indole-positive Proteus and is effective in urinary tract infections caused by these organisms. Two new oral cephalosporin antibiotics, cephaloglycin and cephalexin, which are also not yet available commercially have also been effective in the therapy of some patients with chronic bacteriuria. Acidifying drugs such as methenamine mandelate combined with methionine or ascorbic acid have in some instances, prevented symptomatic recurrences in patients with chronic bacteriuria. The duration of treatment is the most controversial aspect of therapy in chronic bacteriuria. There is general agreement that a two week course of treatment should be given to patients with recurrences due to reinfection, that is infection with a new organism. The same duration of therapy is frequently used in patients with persistent bacteriuria, that is chronic bacteriuria caused by the same organism because of a persistent focus of infection in the urinary tract. However, some workers have noted a higher success rate in these patients when treatment was continued for 6 weeks. Others have not observed improved results when 6 weeks of treatment was compared to the shorter 2 week course. Consequently, the optimum course of treatment in this group of patients must await further investigation.

Hospital Acquired Urinary Infections

These infections are invariably caused by bacteria which show varying degrees of antibiotic resistance. Appropriate therapy is therefore determined by antibiotic sensitivity testing of the organism. Although we prefer to use oral agents whenever possible, in many instances parenteral therapy with an aminoglycoside (kanamycin, gentamicin), polypeptide (polymyxin, colymycin), or carbenicillin may be necessary. Prevention continues to be the best therapy for hospital acquired urinary tract infections. The major cause of these is the insertion of an indwelling catheter into the bladder of a patient with sterile urine because it frequently and promptly results in urinary infection. Approximately 95% of patients treated in this manner develop bacteriuria within 4 days and most of them develop bacteriuria within 24 hours. Furthermore, the acquisition of bacteriuria in patients with open drainage or standard indwelling urethal catheters cannot be prevented by administering systemic antibacterial agents.

Since most patients who require indwelling urethal catheters, need constant drainage of the urinary bladder for short periods of time, that is for periods of approximately a week or less, a number of systems have been studied to determine their effectiveness in preventing the acquisition of significant bacteriuria during these short periods in patients who had sterile urine at the time the indwelling catheter was inserted. The systems (Table 1) can arbitrarily be divided into two groups: *bladder rinses* that cleanse the bladder of bacteria promptly after the bacteria have entered it; and *sterile closed drainage systems* that have been designed to prevent the entry of bacteria into the bladder.

TABLE 1

CATHETER SYSTEMS

1. Antibacterial Bladder Rinses
    a) 0.25% Acetic Acid
    b) Neomycin—Polymyxin
    c) Nitrofurazone
2. Sterile Closed Draining Bags
    a) Non-valve
    b) Valve

Bladder Rinses

The use of constant antibacterial bladder rinses requires a three-way or triple lumen catheter. One lumen to inflate the bag which holds the catheter in place, one lumen for the outflow of urine and the antibacterial rinse, and one lumen which will allow the inflow of the antibacterial rinse into the bladder. The ideal antibacterial solution should be non-toxic, relatively inexpensive, active against all the bacterial species that may be found in the bladder, and unlikely to permit resistant strains to emerge.

Acetic Acid

The use of a 0.25% solution of acetic acid (prepared by adding 2.5 milliliters of glacial acetic acid to 1 liter of sterile water) introduced into the bladder by a constant drip is effective in preventing the acquisition of bacteriuria. This system, however, has definite limitations. For example, the antibacterial effect of acetic acid is lost or greatly decreased when the pH of the urine rises above 5.0. Consequently, the flow of the acetic acid solution must be adjusted so that the pH of the effluent is 5.0 or less and this requires continual monitoring of the urine with pH paper so that the pH of the urine can be maintained at that level.

Neosporin

The next type of rinse contains a mixture of neomycin and polymyxin and is marketed as "Neosporin GU Irrigant." Each vial contains 40 milligrams of neomycin and 20 milligrams of polymyxin which is added to 1 lliter of sterile saline and dripped into the bladder during a 24 hour period. The flow is adjusted to approximately 40 milliliters

TABLE 2

ACQUISITION OF BACTERIURIA AFTER IN-DWELLING CATHETERIZATION IN NON-BACTERIURIC PATIENTS*

Catheter Groups	*Per Cent Infection*
Open Drainage Alone	100
Open Drainage & Saline	100
Open Drainage & Systemic Antibiotics	75
Three-way & Acetic Acid Rinse	20
Three-way & Neosporin Rinse	6
Three-way & Nitrofurazone	20

* Results refer only to patients requiring indwelling catheterization for 10 days or less.

per hour. The general experience with this system is shown in Table 2.

These studies demonstrated further that although neosporin irrigation was very effective for a period of about 10 days or less, the protective effect was greatly diminished in those patients who required indwelling catheterization for periods in excess of 10 days. In addition, neosporin bladder rinse was not capable of sterilizing the urine of those patients who had bacteriuria at the time the catheter was inserted. Nevertheless, neosporin bladder rinse proved to be qupite effective in preventing acquired bacteriuria in most patients requiring indwelling catheter drainage for 10 to 15 days.

Nitrofurazone

A solution of nitrofurazone (Furacin) has also been used as a bladder rinse and is less effective in preventing acquired bacteriuria than the neomycin-polymyxin rinse. Furthermore, a number of patients irrigated with nitrofurazone developed gross hematuria whereas this complication is rarely seen with the neomycin-polymyxin rinse.

Sterile Closed Drainage

Plastic, disposable, sterile, closed-drainage systems require a conventional two-way catheter which is attached, aseptically to the closed sterile drainage bag. There are a number of bags available but the most experience has been with the B-D Asepto Closed System Urinary Drainage Set. This system is effective in preventing acquired bacteriuria in the majority of patients for at least 10 days. Approximately 50% of males and females become infected at 13 and 11 days respectively. The success of the closed system depends upon the utmost cooperation by the hospital staff. The system must be kept closed because sterility will be lost whenever the continuity of the system is broken. The major problem with this system is that there is no way to prevent backflow of urine from the bag into the bladder. Until recently, none of the sterile closed drainage systems available contained a device to prevent backflow of urine. Recently however, we had the opportunity to study a sterile closed drainage bag which contained a flutter valve and which quite adequately prevented backflow of urine. This bag, manufactured by the MacBick Company, Wilmington, Massachusetts, is also made of durable plastic, holds two liters of effluent, is considerably less expensive than the B-D bag, and contains a one way flutter valve at the junction of the tubing and the drainage bag which is most effective in preventing the flow of urine from the bag back into the catheter lumen. This system is equally as effective as other closed sterile drainage systems for short periods of catheterization. Attempts to improve the effectiveness of the closed system by preventing periurethral contamination have been carried out by using either an antibacterial lubricating jelly which is applied to the catheter at the time it is inserted, or by impregnating catheters with antibacterial agents. However, there is little evidence that catheters impregnated with antimicrobial agents or lubricated with antimicrobial jelly at the time of insertion offer much added protection from infection over and above the protective effect of the closed system. One reasonable explanation for this is that the closed system offers its greatest protective effect in the early period after catheter insertion and that this is the same time period that local antibacterial agents would also be effective. Both the impregnated catheters and the jellies lose their antibacterial effect after they are in place for 24 to 48 hours. The use of a closed sterile drainage system combined with a constant antibacterial bladder rinse, such as neomycin-polymyxin has not been found to be superior to the system using "neosporin" antibiotic rinse with open drainage.

Careless catheter usage clearly predisposes the patient to specific hazards, some of which may be life-threatening. Current techniques are readily available either in the form of constant rinsing of the bladder with antibacterial solutions or by the proper use of closed sterile drainage systems which clearly decrease the hazards of indwelling catheters in patients. Our own preference is the use of the neomycin-polymyxin bladder rinse or the recently developed flutter valve closed system. Both are equally effective in preventing bacteriuria for short periods of indwelling catheter drainage. On the basis of past experience, we find it difficult to justify the use of conventional two-way open catheter systems in abacteriuric patients requiring short term catheter drainage. The cost of a good closed drainage system or of an antibacterial bladder rinse is much less than the cost of a course of treatment with most antimicrobial agents.

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Identification of the Tuberculous Infected

George F. Thornton, M.D.

In many ways it is appropriate to start the morning talking about changes related to the problem of tuberculosis. During the 50 years of your hospital's existence there have been dramatic changes, not only in therapy available for tuberculosis, but also in the concept of how to identify the patient infected with tuberculosis.

The changing pattern of tuberculosis is a result of many different factors acting simultaneously. In part, it is the natural history of the disease. Probably the most important factor, however, has been a major change in the socio-economic status of many of our citizens. The availability of effective chemotherapy has also significantly changed the pattern of tuberculosis. However, tuberculosis is still an important health problem. The incidence of tuberculosis is about 20 cases per 100,000 population. Unfortunately there has been little change in incidence in the last decade. This is probably related to significant changes in the pathogenesis of the disease. It is estimated that 60% of all new cases of clinical tuberculosis encountered today are not re-infections or new infections, but relapse of prior infection. The remaining 40% are primarily contacts of the patients with relapse tuberculosis. There have also been some important recent developments in our ability to identify the tuberculosis infected and I certainly will hope to develop this later in the program. Finally, there has been a change in the whole approach to the chemotherapy of tuberculosis with the idea of trying to treat the disease earlier.

I would like to offer a few definitions applicable to all infectious diseases, but particularly easily demonstrated in tuberculosis.

INFECTION represents colonization with viable microorganisms persisting within the host. *DISEASE* occurs when there is some alteration in structure and/or function related to infection. *ILLNESS* is when the patient is aware he is sick. This is very important in tuberculosis. Every person with a positive tuberculin reaction is "infected"

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TABLE 1*

AGE DISTRIBUTION OF PATIENTS WITH BACTERIAL-POSITIVE TUBERCULOSIS

Yr. of Study	*Patients < 50*	*Patients > 50*	*Totals*
1964	83	77	160
1965	64	83	147
1966	70	81	151
Totals	217 (47%)	241 (53%)	458

* Dr. William W. Stead, "Pathogenesis of the Sporadic Case of Tuberculosis, *New England Journal of Medicine*, 277: 1008-1012, 1967.

with viable tubercle bacilli. They may not have tuberculosis the "disease" and may not have tuberculosis the "illness". The man who has a chest x-ray taken for some reason and is found to have bilateral apical fibronodular infiltrates, but is completely asymptomatic, is not only infected with tuberculosis but also has tuberculosis the "disease". Finally, the patient who comes in with a 30 pound weight loss, night sweats, hemoptysis and the full picture of what we think of as clinical tuberculosis, has tuberculosis the "illness". The concept of modern tuberculosis control is to try to spot the tuberculous infected and to treat him adequately before he develops tuberculosis the "disease" and before he develops tuberculosis the "illness".

Dr. William Stead and his colleagues are perhaps most responsible for changing our concepts of the epidemiology of tuberculosis. Table 1 is taken from Dr. Stead's work and shows distribution of the disease tuberculosis in varying age groups. Half the cases of tuberculosis one now encounters are in patients over the age of 50. Tuberculosis is no longer the disease of young children and young adults. Table 2 is also from Dr. Stead's work and provides some of the epidemiologic evidence that tuberculosis the "disease" in the over 50 year age group is a result of reactivation of prior "infection". The change in the age spectrum of tuberculosis the disease and the fact that tuberculosis in the elderly seems to develop as a single isolated case, has led to the concept that approximately 60% of tuberculous disease is the result of reactivation of prior infection. If we are going to make any remarkable changes in the incidence of tuberculosis, we are going to have to try to find the patient *infected* with the tubercle bacillus and institute appropriate therapy before he develops tuberculosis the *disease* and before he develops tuberculosis the *illness.*

There have been some very interesting studies in terms of the use of various skin testing techniques to identify the patient who is infected with the tubercle bacillus and I would like to review some of this work. This has predominantly been carried out by the National Center for Disease Control, Tuberculosis Division. Figure 1 represents experimental work in guinea pigs. One group of animals was infected with human strain tubercle bacilli. A second group was infected with one of the first recognized atypical mycobacteria capable of causing human disease (Battey strain). A third group of guinea pigs was infected equally with Battey strain and with human strain tubercle bacilli. After allowing an appropriate period of time for tuberculin sensitivity to develop, the guinea pigs were then tested with 5 international tuberculin units (standard intermediate strength PPD). This histogram represents the distribution of skin reaction in millimeters of induration at 72 hours. The two groups of animals gave very different degrees of reactivity. The animals infected with human strain tubercle bacilli tended to have much stronger tuberculin reactions. The animals infected with Battey strain had less strong reactions.

These investigators next attempted to separate the two groups by use of a dual skin testing tech-

TABLE 2*

IDENTIFIED EXPOSURE TO TUBERCULOSIS

Group Studies	*Totals*	*Persons With Remote Exposure‡*	*Persons With Recent Exposure†*
Children—primary infection	136	—	112 (82%)
Adults —primary infection	60	—	35 (59%)
Adults > 50 years of age	178	44 (25%)	

‡ > 4 yr.
† Within previous 2 yr.
* Ibid.

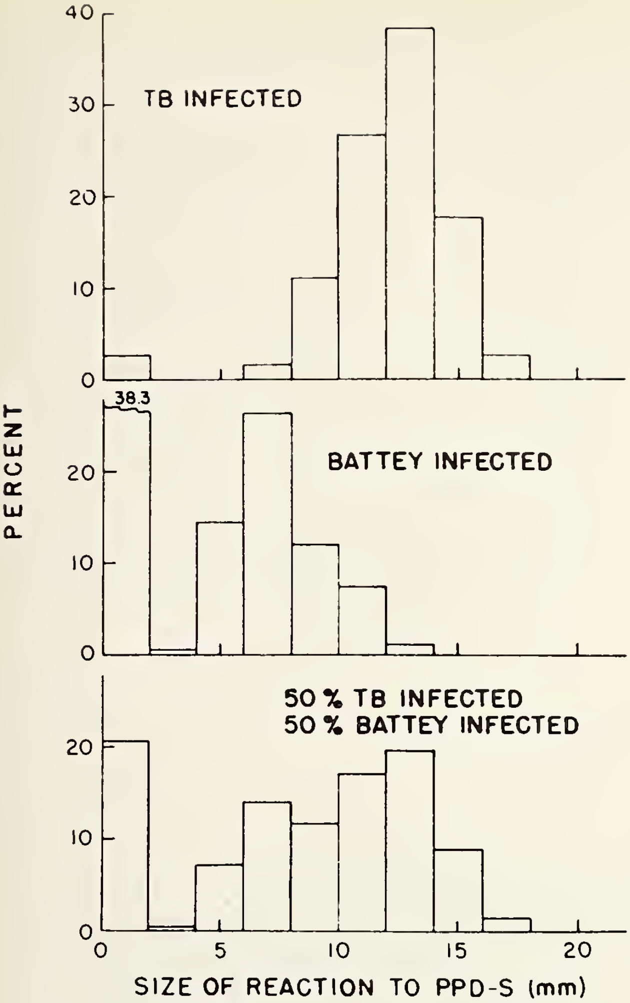

Figure 1*
Reactions to 0.0005mg PPD-S in experimentally infected guinea pigs. (1)

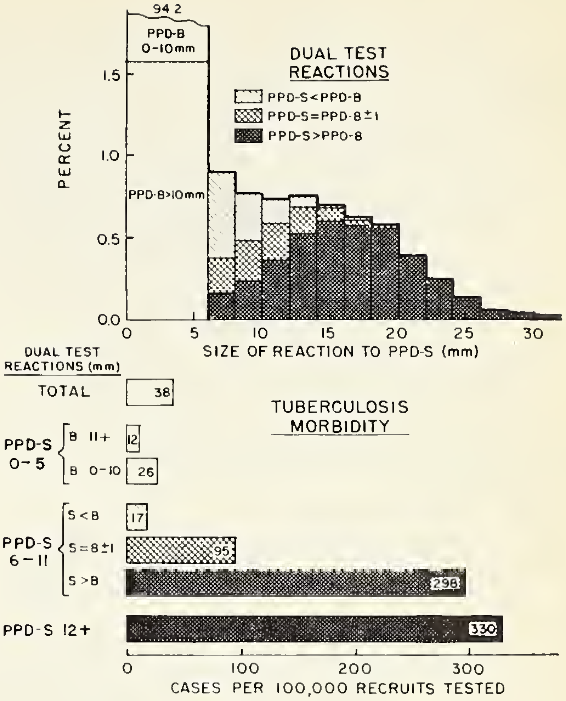

Figure 2*
Reactions of 0.0001mg PPD-S, and tuberculosis morbidity, among 625,000 white U.S. Navy recruits. 1958-1965. (1)

nique using tuberculin prepared from Battey strain (PPDB) and PPDS prepared from human strain tubercle bacilli. They found it was possible using a dual skin test to segregate the animals reasonably well into those infected with human strain tubercle bacillus and those infected with the atypical Battey strain.

Figure 2 shows the results of a dual skin testing technique on a large number of military recruits coming from all over the nation. The results are quite similar to the observations in experimentally infected guinea pigs. Note also the correlation between tuberculin reactivity and subsequent development of tuberculosis. The incidence of tuberculosis was 38 per 100,000 in the entire population. If one looks at the recruits who had less than 5mm of induration with PPDS the incidence was only 1.2 per 100,000. In patients who gave reactions with PBDS between 6 and 11 millimeters of induration there was a much higher incidence of tuberculosis. The highest frequency of all was found in patients who had a stronger reaction with PBDS than with PPDB. Patients who had areas of induration in excess of 12 millimeters with PBDS had an incidence of 330 per 100,000.

This allows us to put together a rational approach to the early identification of the patient infected with the tubercle bacillus before he develops the *disease* or the *illness*. Although PPD preparations made from the various atypical mycobacteria are not commercially available, we have sufficient data to predict with reasonable accuracy infection with human strain tubercle bacillus on the basis of the quantitative tuberculin reaction. The criterion that we accept are that from 0 to 5 millimeters of induration in 48 to 72 hours with 5 ITU (standard intermediate strength PPD) is always a cross reaction. The patient who gives a reaction of 6 to 10 millimeters of induration may be infected with

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* Dr. Lydia B. Edwards, and Dr. Carroll E. Palmer, "Identification of the Tuberculous—infected by Skin Test". *Annals N. Y. Academy of Science*, 154:140-148, 1968.

* Ibid.

TABLE 3

PERSONS RECOMMENDED FOR CHEMOTHERAPY

1. Ex-patients with acute tuberculosis and inadequate drug therapy
2. Patients with x-ray findings consistant with "healed" adult pulmonary tuberculosis and a positive PPD (5 ITU)
3. Documented or presumed conversion of PPD (5 ITU)
4. Strongly reactive PPD (> 15 mm induration, 5 ITU)
5. Persons with positive PPD (5 ITU) who—
    a. Are placed on corticosteroid therapy
    b. Undergo gastrectomy
    c. Have reticuloendothelial disease (Leukemia, Hodgkin's Disease)
    d. Have unstable diabetes
    e. Have silicosis
    f. Have undiagnosed lung lesion
6. Household contacts of active tuberculosis
7. Miscellaneous
    a. Certain pregnant woman
    b. Certain children with measles, whooping cough

either *M. tuberculosis* or one of the atypical mycobacteria. Subdivision of this group require use of the dual skin testing technique. Patients with 11 millimeters of induration or more are always infected with *M. tuberculosis.*

Now that we can identify the tuberculous infected, what should be done about the infection. Here one has to rely on clinical observations and laboratory observations as to the relative risks of developing tuberculosis the *disease* and tuberculosis the *illness.* There are some reasonably good guidelines one can use and they are summarized in Table 3.

The largest group we are asked to see is the patient who has had active tuberculosis in the past but treated in an era prior to the availability of effective chemotherapy. The first really effective antituberculous drug used on a wide scale was INH. Any patient who has never been treated with INH and who has documented tuberculosis deserves a course of INH therapy in order to prevent subsequent reactivation. The second group is the patient with x-ray findings consistent with so-called "healed" adult type pulmonary tuberculosis with a positive tuberculin. The third is the tuberculin converter. The incidence of tuberculin positive is so low in America today that any one in his 20's or younger should be considered to be a "converter" even if there is no prior record of a tuberculin skin test. The fourth group is the patient with a strongly reactive tuberculin (15 millimeters or more of induration with 5 ITU). There is controversy as to why the person with a strongly reactive tuberculin seems to be at greater risk and I think there are at least two explanations. One is that this represents recent conversion and hence the strong tuberculin reaction. However, I think equally acceptable is the concept that anyone who maintains a strong degree of skin reactivity has a continuing potent antigenic challenge: presumably the bacilli are more metabolically active and retain a greater potential to cause disease.

In addition, there are certain groups in whom for theoretical grounds or because of the epidemiology of tuberculosis there seems to be an increased risk. Because of laboratory observations on the effect of corticosteroids on increasing the susceptibility of laboratory animals to experimental tuberculosis, any patient who is being placed on long-term corticosteroid therapy who has a positive tuberculin should be treated concurrently with INH. There is really little clinical data to support the efficacy, or the necessity for this. Nevertheless, I think it is a reasonable thing to consider.

Something that many of our surgical colleagues are unaware of is the known propensity for activation of tuberculosis following gastrectomy. The reason for this is not at all clear. However, I am sure that many of us have seen patients who developed active pulmonary tuberculosis after having had a gastrectomy. A third group are those patients who have diseases such as lymphomas and leukmias, who seem to have an increased propensity to develop tuberculosis.

There are two schools of thought as to how household contacts of active tuberculosis should be handled. One is wait until there is evidence of infection with development of a positive tuberculin before treating. Others would treat all household contacts of infectious cases of pulmonary tuberculosis with INH. The treatment of the tuberculin negative person with INH who is a household contact of an active pulmonary tuberculosis is really the only example of true prophylactic chemotherapy. If one accepts the concept that a positive tuberculin means infection with a human strain of tubercle bacillus, then I would like to think of this as chemotherapy directed at early *infection* with the idea of preventing *disease* and *illness.*

In addition, there are a large group of miscellaneous situations. Women who have had tuberculosis in the past have a very high frequency of activation of the disease in the immediate postpartum period and most feel that pregnancy in a person who has had documented tuberculosis in the past deserves a course of protective chemotherapy.

The same is true of the child with measles and with whooping cough. We do not see either of these diseases commonly any more, but there is a marked effect of measles on delayed hypersensitivity and an association with reactivation. Any child who has a positive tuberculin obviously is a candidate for chemotherapy on the assumption that he is a recent converter. The child who develops measles, and I would also include in this the live measles vaccine, who has been treated in the past with INH prophylactically should receive a second short course (6 months) following measles or measles vaccine. If his tuberculin positivity is found for the first time at the time of his illness, he deserves a longer course.

How long should we treat, and with what drug? I think that 12 months is the minimal period of time treatment of early infection with the tubercle bacillus should be carried out. A single drug is perfectly adequate. We would suggest a single daily dose of 5 mgs/Kg of INH.

In summary, most tuberculosis seen in the United States today is reactivation of a prior infection. The quantitative tuberculin allows for ready identification of the tuberculous infected. Early chemotherapy with INH of high risk patients should be effective in future reduction of the incidence of clinical tuberculosis.

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Subacute Bacterial Endocarditis

Abstract of Discussion

Allan Brandt, M.D.

Abstract of the case presented at the Panel Discussion on May 12, 1971

Dr. Allan Brandt presented a case of subacute bacterial endocarditis caused by Enterococci in a 68-year-old man who had a prolonged, chronic history of pulmonary infection, bronchospasm, steroid administration, intermittent antibiotic therapy and diabetes, as well as arteriosclerotic heart disease and congestive heart failure.

Patient presented with a meningitis which was aseptic and had a downhill course, including progressive congestive heart failure. He expired 12 weeks ofter the onset of his illness and while alive never manifested significant embolic phenomena.

A post mortem examination revealed a 1 cm. suppurative abcess in the posterior cusp of the mitral valve near the annulus. The valve leaflets were free of lesions. There was an endocarditis, as well as evidence of old and recent myocardial infarction.

Dr. Louis Weinstein made the following observations relative to the case:

#1 It is not at all uncommon in Enterococcal endocarditis to have a 12-week course without significant embolic phenomena.

#2 Central nervous system manifestations are extremely common, not only in Enterococcal endocarditis, but other endorcardites as well, and an aseptic meningitis is a common presenting symptom. Indeed, many of the symptoms, such as confusion, lethargy, stupor, are due to showers of cerebral emboli and the formation of mycotic aneurysms which do-not show evidence of invasiveness, since the organism is of low virulence.

#3 The Enterococcus is an organism which fits somewhere between Strep viridans and Staphlococcus in terms of its virulence.

#4 The nature of the host has a great part to play in how well the infection is combatted. In this case the man had diabetes mellitus, steroids, chronic pulmonary history and congestive heart failure, as elements which interfered with the proper response of his body to infection.

#5 The development of a diastolic murmur may represent valve fraying or fenestration, since the Enterococcus not infrequently punches holes through the cusps.

#6 The finding of progressive heart failure may represent the decrease in valvular efficiency secondary to rupture, or decreased myocardial efficiency secondary to showers of emboli through the coronaries causing myocardial infarction.

#7 A suppurative endocarditis which has an electrocardiogram which progresses to left bundle branch block may be due to an abscess of the upper septum as well as ring.

It is hoped that a more aggressive approach in the face of the serious complications of bacterial endocarditis may be taken in the future, such that the valve may be replaced and a septal "patch" may be applied. Certainly there have been a number of successful valvular replacements in the face of subacute bacterial endocarditis with the salvage of the patient and with today's surgical procedures as effectively done as they are, this must be considered more and more frequently.

DR. ALLAN BRANDT, Chief of Staff, Milford Hospital, attending in medicine at Milford Hospital.

Connecticut Medicine

Editorials

A Unified Theory Of Atherogenesis

Many factors have been clinically associated with arteriosclerosis. They are primarily based on statistical evidence, hypertension, the aging processes, wear and tear, constitutional factors are amongst those which appear to be most significantly related to the pathogenesis of arteriosclerosis. Diet, lipid complexes of the blood, smoking, psychic stress and other factors are also related to the pathogenesis of arteriosclerosis. Thus, it appears that arteriosclerosis is of multifactorial origin.

However, a look at the lesion shows them to have the characteristics of scars "tombstones" as Burch calls them of previous injury.[1] The nature of the initial injury remains a mystery and how the actors listed above contribute to the final lesion remains a mystery. One thing is clear, that there is an important element of time here. We find it mostly in older people. Damage due to infection, periodic or persistent elevation in blood pressure, wear and tear, healing scar formation, accumulation of calcium, lipids and other material in the atherosclerotic plaque requires time. Whatever the factors, the longer a person lives the more time such lesions have to develop.

There are three observations already at hand that point to scarring as the primary lesion leading to the atherosclerotic plaque. One is the most recent observation that venous bypass grafts to repair coronary artery obstruction already begin to show fibrous scars, some within a month of the operation. The first experimental observation on this problem was reported by Professor Levin Waters. He injected into rabbits allylamide and produced widespread scarring in the arterial tree which matured into the atherosclerotic plaque in rabbits stuffed with high cholesterol diets after allylamide injection.

Burch[2] studied the etiologic relationship of viral infections to heart disease. He infected mice by intraperitoneal inoculation of encephalomyocarditis virus (EMC) and with Coxsackie virus $B^1 + B_4$. The animals not only developed myocardial and valvular lesions but also invasion of the large arteries as noted by electron microscopy. These two viral infections produce cellular damage to the arteries and could result in lesions which in turn result in scars with healing and ultimate formation of the gross arteriosclerotic lesions of various types, the so-called tombstones of previous injury. These experiments are exact counterparts of the earlier experiments by Waters who used allylamide as the toxic agent.

It is not surprising that arteriosclerotic scars or lesions are limited almost entirely to the arterial vessel even though the virus reaches all cells. Viruses do have the property of selecting special tissues which to invade. Other organisms such as the spirochete produce lesions primarily limited to the arterial vessel. Luetic aneurysms are arterial although the reasons for this localization remain unknown.

The responses to infection and the healing phenomenon vary among animals. It is, therefore, possible that in man many repeated subtle and associated arterial injuries could result in accumulated lesions or damage to arterial blood vessels, especially those with high intraluminal pressure and greatest stresses and tensions on the wall and its anatomic structures. These ever accumulating lesions could result in arterial changes, the scars of atherosclerotic plaques and other relics of previous acute injury.

The many factors, some listed above are in part conditioning factors contributing to the development of arteriosclerosis. Some directly injuring the endothelium, like infections, smoking. Some like conditioning factors that predispose to infection. Some like lipid characteristics of the blood that could influence the nature, extent and rate of appearance of the ultimate plaque as shown in the second part of the experiment by Waters. Obviously, a study of scars could provide some information of the etiologic factors related to the development of the phenomenon. But the initiating and early developmental aspects might be expected to be rewarding and valuable.

Unknown toxins or perhaps those from cigarette smoke can injure the arterial endothelium. Infections could be another. Viruses especially could be one of the more important factors initiating injury which finally results in the state of arterial scars. The final stage could be the lipid character of the blood which leads to increased lipid deposition and ultimate character of the atherosclerotic plaque. Viral infections, one of the most common and universial diseases of man in the production of cardiovascular diseases in man, has not received the attention they deserve.—L.H.N.

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Nutrition, Fat Cells and Obesity

The early period of postnatal life is now recognized as of extreme importance in developing the full potential of the individual. Apparently at birth we are not endowed with all the cellular elements which ultimately form the basis for individual structure and function. The central nervous system consists of a general architecture in the interstice of which grow microneurons up to the age of about 4 years when the full compliment of neurons is reached. During this period of postnatal growth stimulating the nervous system appropriately makes an important difference in the number of microneurons and the ultimate function of the brain.[1]

Now we have learned from Knuttle and his associates[2] that in both rat and man the number of fat cells in the body is determined by the state of nutrition during the early periods of postnatal life. When the subject is overly fed immediately after birth and before cell proliferation or growth ceases the number of fat cells increases and may even exceed 3 times the number in animals that are calorically undernourished or not overly fed.

Once growth and cell proliferation cease the number of fat cells is constant throughout the remainder of life. Once cell number becomes fixed, the quantity of fat stored is reflected in the quantity "stuffed" into each cell regardless of the number of cells.[3] Thus a fat man with 3 times the number of cells can store 3 times as much fat in the body, all else being equal as a man who in early life was not overly fed and in turn has one-third the number of fat cells. Obviously the time to prepare to prevent obesity is at birth and during the period of maturation. Once the number of fat cells in the body is established, variations in caloric intake can vary only the amount of fat stored within the cells but not their numbers.[4]

A man with 3 times the number of fat cells must diet fairly rigidly to reduce the quantity of fat in each cell to one-third of its full capacity. He still would be as fat as the man with one-third the number of fat cells who eats excessively and has his fat cells fully "stuffed." Conversely, the fat man with three times as many fat cells fully "stuffed" with fat would be essentially three times as big as the fat man with one-third as many fat cells fully "stuffed." Thus, the control of obesity would be difficult and dieting would have to be more rigid for the person with three times as many fat cells. To be "skinny" this person's many fat cells would have to contain a lower percentage of fat per cell than those of the man with one-third the number of fat cells.

It would appear from the findings of Knuttle and associates that nutrition during the prematuration period of life that the number of fat cells in the body could explain a large part of why some fat people have difficulty in losing fat and reducing their weight.—L.H.N.

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Inhibition Of Tumor Genesis By Dietary Means

Our knowledge about nutrition and the development of cancer is mostly based on animal experiments and in part on epidemiological studies. Some animal studies have restricted all calories by underfeeding. This has led to inhibition of spontaneous tumors in rats and mice. They showed the lowest incidence and greatest delay in time of occurrence, absence of malignant epithelial tumors and greatest life expectancy. Reductions of both calories and protein depressed tumor incidence to the greatest extent.

Furthermore one interesting finding was uncovered in which the body weight in early life correlated directly with tumor prevalence in later life.

Vitamin A deficiency has been related to the development of odontomas and salivary gland tumors. A cereal type diet low in iodine increased the frequency of thyroid tumors and also led to pituitary enlargement. Magnesium deficiency increased the incidence of thymomas and also chronic myelogenous leukemia. Evidence is also at hand in which choline deficiency leads both to cirrhosis and hepatomas. There is also evidence that associates nutritional factors with modification of the actions of carcinogenic substances.

An example of this last is the carcinogen—azo-dye DMAB which produces liver cancer in rats subsisting on rice. When yeast or liver is added to the diet they prevent the cancer. In addition riboflavin and casein markedly reduces incidence of cancer in rats. If DMAB is demethylated by drug metabolizing enzymes, it loses its carcinogenicity. This suggests that it is the deficiency of protein and riboflavin which depress demethylation and by this mechanism promotes carcinogenesis.

At this point it is well to remember that the endoplasmic reticulum of various organs especially the liver contain enzyme systems which can convert many drugs and foreign chemicals into more polar compounds.[2] Of additional interest is the fact that treatment of an animal with certain drugs causes the animal to acquire an increased capacity to metabolize a wide range of drugs administered later.[3] Genetic and environmental factors play a role but the extent of the drug metabolizing enzymes inducibility appears to be influenced by hormones, dietary and nutritional factors.

Omission of many but not all of the essential amino acids from the diets of rats with Walker 256 transplants and in sarcoma bearing mice inhibits growth of the tumors but also resulted in host loss of body weight. Certain neoplastic cells in tissue have nutritional requirements of L. asparagine and the enzyme L. asparaginase has antitumor activity in neoplasms of the mouse, rat and dog.

A wide variety of human neoplasms have been treated with L. asparaginase derived from E. coli but only lymphocytic leukemia seems to be the most sensitive. With this treatment there are a high percentage of remissions which, however, are not sustained. Amino acid analogs have not proved clinically useful. On the other hand, vitamin analogs especially methotrexate plays an important role in the treatment of acute leukemias and choriocarcinoma that has metastasized.

It can be seen that the inhibition of tumor genesis by dietary means involves a potentially very complex and poorly understood problem. Dietary restriction or specific deficiency leads to many changes in the animal body. With endocrine sensitive tumors such as spontaneous mammary tumors, the principal effect may be related to reduced estrogen production. Or a general phenomenon may be involved, one secondary to a decrease in the mean metabolic activity of the tissue. Finally, a deficiency in an amino acid essential for growth of some tumors such as L. asparagine can also be a limiting factor. In any event, experimental observations on animals it is hoped, will finally promote sustained study in man.—L.H.N.

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Electric Enhancement Of Bone Union

Lavine and his colleagues[1] describe the first case of human congenital pseudarthrosis of the tibia successfully treated with a direct electric current. They employed their method previously shown to be effective in rabbits. They placed electrodes at each end of an experimental lesion in rabbit femora and demonstrated that direct current in the range of 2-4 μa increases normal healing by a factor of 2 when compared with nonstimulated controls. Pseudarthrosis is a rare local dysplasia in which there is virtually no possibility of effecting union by conventional methods.

Their patient was a 14 year old boy who needed braces until age 4 at which time he underwent a surgical repair by bone graft which healed the defect. However, at age 11 he fractured through the old pseudarthrosis site which never healed again regardless of repeated surgical tries. The only alternative left was amputation. It was at this time Lavine decided, based upon his experimental observations on rabbit femora to try a direct current across the pseudarthrosis defect.

The current was passed through the area by inserting platinum electrodes proximal and distal to the area of nonunion. The electrodes were so arranged that the current path was made to pass bony tissue on each side of the defect. The external current for the power supply consisted of two D cells (3 volts in series). The potential difference across the electrodes was .55 volts. During the entire treatment period of 125 days the current was applied at least 92 percent of the time. Except for extremely brief checkout periods the polarity of the distal electrode was left positive and uniform during the treatment period. Four months after electrical treatment the area was surgically inspected, a biopsy taken. No motion on manipulation was found at the pseudarthrosis site. Histological studies revealed beginning bony union.

It is clear that electrical potentials play an important role in directing the architectural and structural development of bone. Thus, success of applied electric currents in treating this difficult orthopedic condition certainly warrants its application to other less rare problems such as nonunion and delayed healing of fractures.

Obviously there are further ramifications. Understanding the mechanisms linking electricity to basic cellular phenomena represents a problem of primary biophysical importance.

To be sure, this is but one case. However, the foundation of this report rests upon prior animal experimentation. The procedure was tried on the most difficult problem in bony union and the most rare. However, here there was no other alternative except amputation, a grave and mutilating procedure. The difficulties presented by this disease represents an extreme test case of the value of electrical stimulation. It should now not be difficult to apply the method in other situations of nonunion and delayed healing of fractures.—L.H.N.

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Chinese Medicine

A picture of medicine on mainland China is emerging. Among the latest physicians and scientists to visit China is Victor W. Sidel, Professor of Community Health at Albert Einstein College of Medicine and Nobel laureate, Dr. Chen Ning Yang.[1] Dr. Sidel explained how a physician is trained. No one simply decides to be a physician. A Chinese youngster's school days begin at seven and usually lasts for ten years, five in elementary school and five in high school. After that he works in the factory or farm commune for three to four years although some go into military service instead.

It the young person displays what officials call selflessness and various qualities suggesting he or she could use further education to benefit the entire Chinese society, Dr. Yang translates this as "good public relations", co-workers may then nominate him or her for medical school. Here he or she usually spends six years. Emphasis now is on shortening the curriculum by as much as fifty percent. Once in a medical school the student, equally divided between the sexes, receives no examination or grades. The emphasis is on cooperation rather than competition among the students. It is considered a great honor to go to medical school because of the faith and confidence fellow workers have in the nominee. Medical students, as are most physicians who practice in cities, are expected to work and train part-time in rural areas.

Dr. Sidel reports that the Chinese are very much abreast of what's going on in medicine throughout the world but they are concentrating less on sophisticated procedures such as open heart surgery and paying more attention to the day-in and day-out care of the 600 million people living in the countryside as well as the 150 million city dwellers. They appear to view medicine as a part of the whole effort of the society to improve itself. As a part of this mobilization of resources much of the initial screening of patients is done by "barefoot" doctors, farm commune workers with about three months training at a hospital. Then there are "factory doctors" similarly trained production workers and Red Guard doctors, housewives who get about ten days training and are then taught "on the job" by regular physicians. These paramedical workers also have a health education role and maintain medical records including the type of contraceptive used by each woman in a city "lane" of households.

Officials claim the birth rate in some cities such as Shanghai now is down to 6-7 per 1,000 population. In rural areas it is said to be 18 or 20 per 1,000. The two observers never saw a lock in China except on the medical kit of a "barefoot" doctor to keep childern from harming themselves.

Chinese physicians are well aware of antibiotics, use them when indicated and also use herbs if for example a pneumococcal pneumonia is accompanied by pain. Acupuncture represents the combining of traditions and todays medicine. The procedure is based on the theory that inserting needles into one part of the body affects bodily processes elsewhere and this has been practiced for 2,400 years. Acupuncture anesthesia, however, is relatively new and still under study. Dr. Sidel was told that it appears to work better "above the waist" (diaphragm). However, in addition to witnessing a chest operation successfully carried out by acupuncture anesthesia, he also witnessed removal of an ovarian cyst in a patient under this anesthetic. Preoperative preparation was quite similar to that used in American medical centers.

Chinese efforts have been particularly strenuous against venereal disease, "emphasizing prevention not so much for the sake of the individual as for the entire society." Efforts against alcoholism and drug abuse appeared to Dr. Sidel to be successful although the Chinese are still smoking cigarettes by the tens of millions.

Chinese physicians are reading the world's medical journals but are not publishing their own, because they are trying to devise means of reporting medical science and clinical applications without at the same time glorifying individual physicians or institutions. There is a tendency to criticize anyone who attempts to set himself apart or thinks himself better than others. This philosophy seems to concern not the individual so much as the entire society, a philosophy they attempt to instill from early childhood. Children are taught from the very beginning that if, for instance, one of them falls down, it is the responsibility of the others to help him to his feet and make certain he is alright.

In the November issue of *China Medicine* an anonymous article reports the successful restoration of a youngster's accidentally amputated arm. The article included a detailed description of debridement, fixation of bone fragments anastomoses of blood vessels and nerves suturing of muscles and postoperative management. This procedure as well as other earlier successful limb reimplantations in Chinese hospitals were characterized as "victories of Mao Tse-tung's thought." Dr. Yang explained "they feel that they owe everything to Mao especially their self-reliance. There is some merit to this the Chinese surgeon interceded, "I was born in a peasant family. In the old days I never would have had the opportunity to train as a surgeon and do procedures like this. Chairman Mao gave me the chance."

One would almost think that the Chinese have appropriated the Oath of Geneva into their medical philosophy. For do we not all take an oath on graduation to dedicate our lives in the best interest of the patient and in the service of humanity? This is, after all, the goal of medicine everywhere regardless of the political system.—L.H.N.

Reference

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Cerebral Atrophy In Young Cannabis Smokers

(*Lancet* I:374, February 12, 1972). On December 4th *Lancet* published a paper by Campbell and his colleagues reporting brain damage in cannabis smokers. Now Conrad J. Swartz considers further the symptoms of cerebral impairment using the mental status examination and functional inquiry. These symptoms indicate that the effects of cannabis persist beyond the obvious period of acute intoxication in keeping with the findings that cannabis remains in the body for 3 days and its metabolites for 8 days.

These include impairment of memory, concentration, attention and time sense; mood swings particularly irritability, euphoria-like contentment in the presence of reduced external stimuli in relation to work capacity, study habits and life style; a paranoid stance; and physical complaints—for example, respiratory and gastrointestinal conditions and persistent thirst.

On being asked about the above the user may wonder out loud that perhaps cannabis is doing other things to him that he had not previously realized. He will usually have seen some of these symptoms in his cannabis-using friends. If he can accept a trial of discontinuation of use for 2-3 weeks he will then often indicate that he is somehow feeling better, thinking more clearly and picking up some of his old interests. This insight may lead to abstinence or reduced usage. Some patients, however, while admitting symptoms will insist that the dysfunctions are of no importance to them, because of their philosophical attitude to competitive society.

It has been agreed by some that this clinical evidence suggests that the symptoms are related to a long-acting toxin in cannabis and that they clear strikingly when its use is stopped.

This view is supported by the unusual phenomenon of reverse tolerance which may indicate that a person who uses cannabis often enough is only "tapping up a partially empty gas tank." While this may be so in the early stages of regular use, actual tolerance to cannabis does seem to develop in some users as shown by an increasing preference for hashish which is 8-10 times stronger than marihuana and by the enormous doses consumed by some patients described by C. J. Minas in the *Int. J. Psychiat.* 9:533, 1970-1971.

Such a change in metabolism in the brain could result in the toxic mechanisms being replaced by more permanent changes such as those described by Campbell above.

Finally, the similarity to encephalitis lethargica is striking enough for one to wonder about the extent of medical prescriptions of cannabis products in the treatment of epidemics associated with this condition during a surprisingly brief clinical heyday from 1915 to 1926.[2]—L.H.N.

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Photochemical Smog

Measurement of oxidant in the atmosphere has been used for some years in this country as an indicator of the occurrence of photochemical air pollution in urban environments. Levels of oxidant, chiefly ozone in excess of 10 parts per hundred million (pphm.) are considered to be evidence of photochemical smog formation. In comparison, clear air ozone levels vary from 2-5 pphm. during daytime and falling to zero at night. The photochemical smog reaction takes place when unsaturated hydrocarbons and oxides of nitrogen in the presence of sulphur dioxide is oxidized to sulphuric acid.

A typical British car emits about 8g/mile of hydrocarbons, 2.5g/mile of oxides of nitrogen expressed as NO_2 and burns fuel containing .08g of lead per mile. About 20 percent of the lead consumed is emitted as particles small enough to remain airborne for a significant length of time. Thus, there is no doubt that motor vehicles are the principal outlets for photochemical smog in large cities for they are the sources for the unburned hydrocarbons, sulphur dioxide and also smoke.

Meteorological conditions are important, for the sequence of reactions leading to photochemical smog requires also the production of significant ozone concentrations sufficiently near the ground for the unburned hydrocarbons not to have been dispersed by diffusion or by wind. But even so, formation of photochemical smog in large cities of North America has been a striking proof of the formation of ozone at surprisingly low levels in the atmosphere. This has just been shown by Atkins, et al.[2] They found that ozone concentrations do occur near the ground and that the background concentration is easily dispersed but varies between 20-40 pphm.

The same measurements have, however, shown that when meteorological conditions are suitable and in particular when winds are light, then concentrations of ozone near the ground may be three times as much or more. They demonstrated further that the excess ozone comes not by diffusion downwards through the troposphere but is formed locally. Obviously the concentrations now reported from rural Harwell[1] are much smaller than those which have recently been found for Los Angeles where the greatest concentration of ozone measured at Harwell are exceeded on half the days in the year. Here concentrations as great as 580 pphm. have been recorded. Even so, it is a surprise to say the least that even in the countryside in England the air can be so affected.

Of course, it is no surprise when concentrations of ozone as great as 80 pphm. are recorded, that unburned hydrocarbons and NO_2 should conspire to oxidize sulphuric acid. The result is not merely that ordinary air becomes foul and even unbreathable but that sulphuric acid in combinations with drops of water and particles of dust and smoke creates the peculiarly smoky kind of atmospheric turbidity through which the inhabitants of large cities are forced to see.

The precise implications of all this for the control of photochemical smog in large cities where it is a public nuisance and serious health hazard are not easy to define but there can be no doubt that the controlling element in the sequence of events producing smog is the presence of unburned hydrocarbons in motor vehicle exhaust. We cannot expect that ozone will not be found on sunny days even in temperate latitudes. The remedy, if any, is for drastic reduction in the use of the internal combustion engine and for the designers of such engines to give us cleaner exhaust.—L.H.N.

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Suicide: A World Problem

A conference on suicide prevention was hel‹ in Mexico between December 5th—December 8th by the International Association for Suicide Prevention, who gave an international perspective to this serious problem. It seems that about 1,000 people will kill themselves every day according to WHO.[1]

In his presidential address, Professor Irwin Stengel said that it was time to take stock of the basis of the subject and define suicidal acts more precisely so as to allow valid international comparison. Definition by motivation was unsatisfactory because the patient may not be aware of his motives. Conflicting motivation also make classification by "appeal", "escape" and "manipulation" difficult. Furthermore, such terms as parasuicide, and pseudosuicide are being used differently by different workers.

Most "attempted suicides" were wrongly thought to have intended nothing of the sort. With successful suicide only a minority of the acts were done with a virtual certainty of success. People wanted not so much to live or die as to do both at once in differing degrees with a small minority at either end of the life/death spectrum. Stengel believed that the definition of the suicide act which caused the least difficulty was "any deliberate act of self-damage which the person committing the act cannot be sure to survive."

Aside from statistical doubts useful information emerged from different countries. In Argentina, the mean age for suicide in 1925 was in the 15-20 age group, in 1968 it was in the over 65 age group. This trend had paralleled industrialization and urbanization and the decrease in the size of the family. In Finland there were high rates for depression, suicide alcoholism, and violent crimes. The ratio of male/female suicide was 3:1. In Helsinki, however, where half of the population lives, it was 2:1 and especially high among working women.

The lowest social classes had the highest suicide expectations. In India, suicides tended to be concealed because of the legal position and religious taboos. Nevertheless, the act was sanctioned by the Jain religious order and since Gandhi, has been used as a religious weapon. In Italy too, family and social pressures led to under reporting of suicides. Dr. Maurice Farber pointed to the factors which discourage suicide: moral condemnation, intense family loyalty, social tendencies to intervene in the affairs of others, the concept of "patients" and a genius for making the surface of life attractive by ignoring the dismal realities below.

Suicide was especially likely in people faced with intense demands on personal giving which might prove too much to bear if the pressures were irresistible. Suicide rates have been notably high in groups who had migrated from areas of poverty and unemployment in the south of Italy. Alienated groups such as Women's Lib and other minorities discriminated against also showed high rates according to Dr. Santiago Mar-zuniga chairman of the organization.

In Israel contributors reported the suicide rate had gone down and was now highest in Eastern European Jews, an older group than others. Attempted suicide and deliquency were highest in African and Asian Jews, median in the native born and lowest in those of European origin, just the reverse of the suicide figures.

Holland had had a static low rate of 9.5 per 100,000 for 80 years with a male to female ratio of 2/3 and no urban/rural differences. The Dutch attitude was that everyone has the right to live and it is our duty to make society a place where everyone can live happily. Attempted suicide was treated with compassion.

Apart from Great Britain and Israel it emerged that Japan was the only country where suicides had come down. For centuries there had been no taboo on it. But as feudalistic altruism was replaced by Western individualism so also did suicide decline. In Great Britain the Samaritan organization seemed to have played an important part in the decline in suicide by about a third between 1963-1969. Two-thirds of the British population had accurate knowledge of what Samaritans were and two-thirds of these would be willing to seek the organization's help if need be.

In this country there are more than 200 suicide prevention centers but these have been much less successful in attracting trained volunteers and in making their services known to the public. A paper from the Los Angeles Suicide Prevention Center has done much of the scientific work on suicide in the past 25 years, described a predictive scale which had correctly forecast suicide in 29 of 31 men over forty from a total of 1,049 men who had lapsed from contact for 2 years. The scale had proved least accurate with young female clients of the center.

In the San Francisco Suicide Prevention Center, 1,752 clients had been separated into "treatment" and "no treatment" groups. The first group was systematically followed up by telephone calls or letters for 4 years, and the second not contacted at all. The expression of continuing interest seemed to make no difference in the suicide rate (1.5 percent in each group). Their finding, however, runs contrary to those of self-injury in Sweden and England.

That self-injury is far commoner than has been recognized was strongly suggested by a survey in London, Ontario, a town of 200,000 population. Information of all kinds of hospitals nursing homes, doctors, welfare agencies and the county jail gave a recorded rate of 730/100,000 per year and an estimated true rate of 1,433.

This remarkable result of 1 in 70 of the population per year is more than 17 times the reported figure by Parker and Stengel in Sheffield and will doubtless spark off similar studies elsewhere. Clearly the suicide problem is important, more so than the reported figures would indicate and needs urgent attention everywhere.—L.H.N.

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Some Developments In Nuclear Medicine

Information about the heart and its vessels is widely obtained by means of selective contrast angiography and cardiac catheterization. This method gives excellent resolution of vessels and yields precise information on pressure and stroke volume. Radionuclide techniques, however, are simple, safe, rapid (10-30 minutes) and non-invasive. Radioactivity can be followed when blood vessels become too small for visualization and the dose of ^{99m}Tc and Zenon and ^{13}C ammonia is much smaller than that for the conventional roentgenogram.

The radionuclide of choice has been Technetium 99m and the investigators use the scintillation camera which along with the short-lived radionuclides helped to revolutionize nuclear medicine a few years ago. Changes in techniques and instrumentation occur almost daily and auxiliary equipment now usually includes computers.

Radionuclide angiography can serve as a first line screening procedure such that negative findings will eliminate the need for further studies such as cardiac catheterization. It can detect left ventricular aneurysms. It has an important use in congenital heart defects. Intracardiac shunts can be detected by administering two radionuclide sequentially. In this way, it is possible to distinguish clearly between the right and left sides of the heart and derive time-activity curves for passage of the labeled compounds through the heart.

Two radionuclides are used because in many congenital heart defects enlargement and malformation or rotation of the heart makes it difficult to distinguish between the right and left side as seen in the frontal or left anterior oblique view. This is alleviated by using two radionuclides with different localizing properties. Zenon^{133} is first given I.V. then a minute later ^{99m}Tc is administered through the same needle. The Zenon passes through the right side of the heart and goes to the lungs. In most normal persons, most of the radionuclide is washed out within 10 seconds and its appearance in the left side indicates a right to left shunt. Technetium 99m stays in the vascular system enabling imagery of the right heart, lungs and left heart. It appears in the left heart at the same time as it is first seen in the right heart. This indicates a right to left shunt.

This can all be taken down on tape and played back at any time. In time, information on the size of the shunt becomes available in addition to present data on shunt direction and level.

Results of this technique have been confirmed in 29 out of 30 patients by catheterization and angiography.

Another development in nuclear medicine is ammonia ^{13}N, a gas with a half life of 10 minutes. This new metabolic tracer will facilitate greatly improved studies of the myocardium because it is incorporated in the synthesis of adenosine triphosphate (ATP). Accordingly, with this radionuclide, one can study directly cardiac metabolites, whereas radio labeled K only allows study of ion-movement in and out of the cell. Because of the short half-life of ^{13}N ammonia, it produces less than one third of the radiation dose of a simple X-ray. ^{13}N ammonia is a positron emitter and gives a count rate per dose with the scintillation camera. Ongoing ATP indicates normal myocardial metabolism, because ATP is synthesized in the heart and ^{13}N ammonia myocardial uptake is via ATP. It can be used in study and clinical evaluation of myocardial infarction. A "hole" in the myocardial image produced by labeled ammonia would signify interrupted metabolism and, therefore, an infarct. The labeled ammonia certainly will be extended to the study of metabolism of other organs including the brain.

The screening techniques mentioned above will be most useful in hospitals without cardiac catherization equipment and certainly it will eliminate the need for cardiac catherization and contrast angiography in an increasing number of patients. It has not as yet been perfected for use in the newborn and small children.

At a recent symposium on nuclear medicine, Dr. Joseph Kriss of Stanford University, reported on over 40 patients. It enabled him to demonstrate markedly abnormal and distinguishable scinti photographic patterns in a variety of specific cardiovascular disease including both congenital and acquired heart disease involving both right and left sided lesions, diseases of the great vessels, and pericarditis. They also found this method a means of following the effects of medical and surgical interventions.—L.H.N.

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The Problem-Oriented Medical Record

Until recently there has been no body of literature on the structure and content of medical records. There has been, therefore, no framework within which such a description could develop, no rules against which performance could be judged, no basis from which to teach scientific methodology. When the burden of disease was acute as it was a half century ago the medical record was of minor importance. Physicians kept records solely for themselves, bound them into personal volumes and from these emerged many of the classic descriptions still valid to the present. Perhaps it is this heritage that is the fundamental reason why the medical record has defied change and in style remains a fragmented narrative inappropriate for describing anything other than a discreet episodic illness. Experience with computers and records has been disappointing. The many recorded failures suggest that we have failed to define objectives or to define the basis on which to build.

Feinstein[1] points out that the clinician uses three types of data to make decisions about the past, present and future by determining a diagnosis. The first describes the disease in pathological or biochemical terms and are derived from investigative procedures. The second type of data describes the host and include personal and social factors. The third describes the illness that occurs in the interaction between the disease and its environmental host. These data consist of clinical phenomena, the host's subjective reactions or symptoms and the disease's manifestation or signs. Such a diagnosis may most usefully be defined as a summary of hundreds of observations in one or two words. As for a rational procedure of classifying the data of human illness, the behavioral phenomena associated with illness, the method has so far eluded us.

Lawrence Weed[2] in his book presents the thesis that the record is not a static repository of medical observation structured in the meaningless order of their source, but a precise instrument of communication, one that must serve the patient, since the patient is likely to require services of many physicians and as far as possible, the progress of the patient among them must be easy and without confusion; record that must serve the experienced physician and yet be intelligible to the medical student; one that must serve the student, yet not frustrate the practicing physician.

Weed proposes a technique of clinical record keeping which organizes the patient's record in a logical and efficient manner. In essence, he proposes the creation of a problem list. By enumerating a patient's problems it becomes possible to prepare a full list of plans, both diagnostic and therapeutic, and to compare progress notes keyed by number to the original list. The technique is designed for problem solving. The initial list may reveal problems in various stages of resolution and plans created for each problem constitute a series of networks.

Thus the critical paths within the program of care can be discerned. When a problem is solved this is indicated so that the complete problem list becomes an accurate, up-to-date summary of the patient's medical status. Superficially, the problem list may seem to be no more than a list of diagnosis as at present compiled, so that what is being proposed is only a more sophisticated structure for recording.

Weed advises that the problem list should state problems at a level of refinement consistent with understanding, from precise diagnosis to the unexplained finding. He asks that the student understands a problem and is honest in defining it, no matter how elementary the terms required. Behavioral and social problems must be defined no less precisely or honestly. Implicit in the problem oriented approach to the organization of data in the Weed record is the necessity for completeness in the formulation of the problem list with careful analysis and follow up of each problem as revealed in the progress notes.

As a part of these progress notes a further refinement proposed by Weed is the application of flow charts to problems inadequately described by narrative. Physical findings, laboratory investigations, treatment and other data varying over time can be interpreted more easily if displayed in such a way that any relationship can be seen. The concept of networks, flow charts and critical paths appear to be just as relevant to medicine and the care of the individual patient as in any other decision making process. The problem oriented record has been commented on enthusiastically. It is seen providing the means for improved patient care, medical education and research.

It is possible, of course, as Hurst comments[3] that in the application of the system to hospital records it might encounter opposition to change, disagreement over format, and resentment of the educational process. He comments that not all individuals involved shared the same degree of interest. Others saw no need for change. While few even regarded it as a primitive exercise. However, he does not provide any evidence on which to evaluate the Weed system. Even though the potential benefit to patient care and education are obvious, nevertheless, the introduction of a new system could be facilitated if one can show objective evidence of benefit.[4]—L.H.N.

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Clinical Correlations With Coronary Arteriography

(*Virginia Med. Monthly*, 97: 688, 1970, Newton, R. M., et al.) The authors performed coronary arteriography to attempt a correlation of coronary artery disease with the double Masters tests. They found among 31 of 43 persons in the abnormal 20 percent false positive and 50 percent false negative. One has to achieve a rate of 130 to consider the exercise adequate.

Of the 43 patients in the abnormal group 13 had normal resting ECGs.—L.H.N.

Latent Herpes Simplex Infection

(*Nature* 235:312, February 11, 1972). Many people infected with herpes simplex periodically and often predictably suffer from recurrent herpetic infections in response to physical or emotional stimuli and the resulting lesions always appear in the same part of the body.

Clearly this virus must persist in infected individuals but which cells harbor the virus between eruptions? Indirect evidence incriminates the sensory ganglia and cells associated with nerve trunks as the reservior of the virus.

In *Nature's New Biology* for February 16th, Stevens, Nesburn and Cook have now brought forth evidence in support of this view. In rabbits infected with the virus, it latently infects the trigeminal ganglia and the virus can be recovered when nerve cells are cultured in vitro.

If herpes simplex can latently infect sensory ganglia of rabbits the same may very well be true of man. In other words, sensory ganglia are probably the site of the reservoir of herpes simplex virus in presistent infection of man.—L.H.N.

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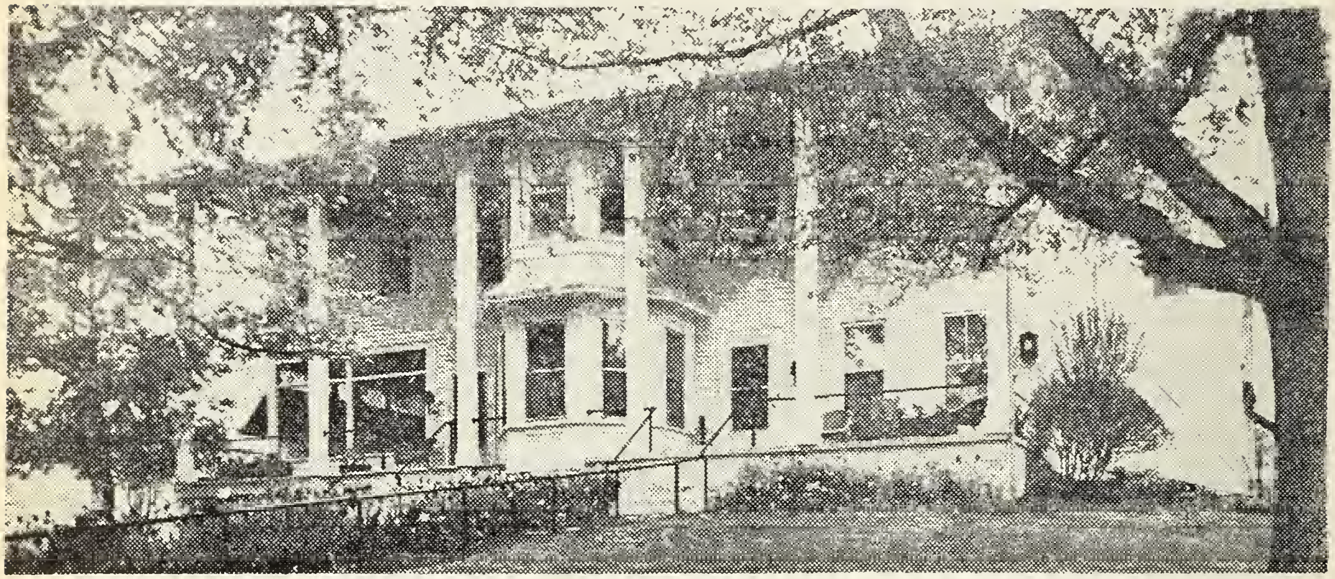

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SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, April 5, 1972

I. Attendance

Present in addition to the Chairman, Dr. K. F. Brandon, were: Drs. Weber, Cramer, Spitz, Backhus, Nolan, Granoff, Dean, Gardner, Fabro, Hess, Rem, Johnson, Harwood, Pelz, Ragland, Jr., Roch, LaBella, Root, Jr., Freedman, Dambeck and Klare.

Also present were: Mrs. Lindquist, Mr. Sullivan, Mr. Tomat, Mr. Bugan (AMA), Dr. Flom (COMPAC), Associate Dean Fleeson (UConn Medical School) and Dr. Richards.

Absent were: Drs. Grendon, Bradley, Wilson, Palomba, Nemoitin, VanSyckle, Friedberg, Luby, Harkins and Sprecace.

II. Routine Business

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Harold W. Higgins, 7 Clinic Drive, Norwich (NL), 1/1/72
Frank J. Raffaele, 159 Main Street, Stamford (F), 1/1/72

Date of Next Meeting

In accordance with the Bylaws, the President will call the 1972 organizational meeting of the Council "as soon as possible" after the annual meeting of the House of Delegates on April 25. The first order of business at the organizational meeting will be to elect a Chairman and Vice-Chairman for 1972-73.

III. Old, New and Special Business

Report—Committee on Public Health

It was VOTED to receive for filing a report of the Committee concerning the subject of Public Health Code regulations re the use of out-of-state, unregistered clinical laboratories by Connecticut physicians and the billing of physicians directly for laboratory services rendered to patients. It was further VOTED to adopt a subject resolution contained in the report as follows:

WHEREAS: It has been called to the attention of the Council of the Connecticut State Medical Society that some physicians have been violating Section 19-13-A of the Connecticut Public Health Code in that they have been utilizing out-of-state clinical laboratories not registered in the State of Connecticut, as well as Connecticut laboratories lacking such registration; and

WHEREAS: Some laboratories, both in-state and out-of-state, have been violating Section 19-13-D of the Connecticut Public Health Code by billing physicians directly for laboratory services without furnishing patients a statement of actual laboratory charges for such services; and

WHEREAS: The above-described practices may lead to legal action being taken against physicians accused of such violations, with a consequent increase in the cost of malpractice insurance to all physicians; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society arrange to have publicized among the members of the Society the Public Health Code regulations applicable to these practices and the penalties assessed for their violation and inform the Connecticut Public Health Council of this action.

Communication—President, Hartford County Medical Association

It was VOTED to receive for filing two related communications received from the President and the Executive Director of HCMA which proposed that the Council consider petitioning the private insurance carriers, through the Health Insurance Council, to write service benefits and other types of full-pay contracts, based on fee schedules already would be competitive with similar contracts already being offered to the people of Connecticut by Connecticut Medical Service, Inc. It was further VOTED to refer these communications to the Committee on Third Party Payments for study and report to the Council, with the notation that if such a petition were to be made it would require an action by the House of Delegates to rescind the present policy advocating "usual, customary and reasonable charges" and adopt a policy advocating "fee schedules" as the preferred basis of third party payment for physicians' services.

Communication—Board of Governors, NHCMA

It was VOTED to receive for filing a communication from the NHCMA Board of Governors which proposed that the Society undertake an educational program for the membership that would "specifically concern itself with the dangers to physicians, patients and the practice of quality medicine which are inherent in certain insurance programs." It was further VOTED to refer this proposal to the Committee on Third Party Payments for study and report, with a note of caution expressed that an education program which pointed out "dangers" inherent in a named third party payor might pose undesirable legal problems for the Society.

Reports—Committee on Third Party Payments

It was VOTED to receive for filing four reports submitted by the Committee and to act upon them separately as follows:

(a) *Concerning the 1971 CSMS Relative Value Guide*: To adopt and implement a resolution recommended by the Committee as follows:

"WHEREAS: The 1971 CSMS Relative Value Guide has now been published and distributed to the Society's members; and

WHEREAS: The coding and terminology of the 1971 CSMS Relative Value Guide are similar to the coding and terminology used in the 1969 California Relative Value Studies and the AMA Standard Terminology; and

WHEREAS: Twenty-nine or more state medical societies have officially adopted such coding and terminology; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society strongly recommend to all third party payors in Connecticut that they standardize on the coding and terminology of the 1971 CSMS Relative Value Guide as soon as feasible, and discontinue use of the 1964 California Relative Value Studies as adopted by the Connecticut State Medical Society in 1965."

It was further VOTED that, in particular, the Liaison Committee with the State Welfare Department is urged to discuss with the State Professional Policy Committee or the Welfare Commissioner the desirability of replacing the present Welfare Department's RVS (as a basis for calculating payments) with the 1971 CSMS Relative Value Guide.

(b) *Concerning Statutes re Immunity of Members of Hospital Utilization Review Committees*: To approve a recommendation of the Committee that changes be sought in the Connecticut statutes providing immunity from civil suit of physicians serving on hospital utilization review committees which would eliminate the contingency of "without payment" and would extend the same immunity to physicians serving on utilization review committees of other types of institutions such as extended care facilities; also, that thought should be given to making provision for similar immunity for physicians (and perhaps non-physicians) who may be serving on areawide review bodies, such as the Bennett Amendment's PSRO calls for, in the event that such legislation may be enacted. It was further VOTED to refer this report to the Committee on State Legislation for implementation at the next appropriate session of the General Assembly.

Progress Report—CSMS Efforts to Clarify Member's Hospital Staff Status

It was VOTED to receive for filing and to acknowledge a letter of thanks from a member on whose behalf the Judicial Committee and the Council had made efforts to assist the member in obtaining reasons in writing from a hospital's medical board or governing body as to why his request for a promotion to attending staff status was being denied. The member advised the Council that the matter has been resolved and that he has received promotion to attending staff status.

Report—Liaison Committee with the State Welfare Department

It was VOTED to receive for filing a report submitted by the Committee on the matters discussed at a meeting held on March 15, 1972. In particular, the Committee reported that it had not yet been successful in arranging a meeting with the State Professional Policy Committee to review with the PPC a number of matters relating to the Medicaid program, as requested by the Council.

Request—Appointment of Representative to Family Planning Council

In response to a request from Commissioner Foote that the Council appoint a representative to serve with the Connecticut Family Planning Council, it was VOTED to request LeRoy H. Wardner, Hartford, to accept Council appointment to this post.

> *"The history of science, and in particular the history of medicine . . . is . . . the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."*
>
> *– George Sarton, from "The History of Medicine Versus the History of Art"*

Should nongovernment scientists and physicians play a role in drug regulation?

Opinion

Results of a questionnaire to 7000 physicians:

82.8%
Physicians should play a role

78.3%
Independent scientists should play a role

69.8%
Medical academicians should play a role

Opinion & Dialogue

Dialog

Should nongovernment scientists and physicians play a role in drug regulation?

Doctor of Medicine

Herbert L. Ley, Jr., M.D., M.P.H., Formerly Commissioner, F.D.A. (1968-1969) Currently Medical Consultant

In order for drug regulation to be effective, participation in the regulatory process from nongovernment physicians and scientists must be encouraged. Without such involvement, there will continue to be a high degree of controversy surrounding any regulations promulgated by the Food and Drug Administration.

There are two areas in which participation and communication by nongovernment physicians and scientists could significantly improve the process of regulation. First, scientists and physicians throughout the country could become involved in consulting relationships with the Food and Drug Administration in important scientific areas while regulatory policies are being evolved. If nongovernment professionals could bring their expertise and experience to bear early in the decision-making process, they would have less reason to criticize the final outcome.

Secondly, practicing physicians, academic physicians, and academic-based scientists could make it their business to comment on proposed regulations appearing in the Federal Register. Ideally, a system could be instituted whereby medical, scientific and technical people could see the Federal Register regularly, and provide the Food and Drug Administration with a body of opinion that has so far gone unheard. The FDA is caught among pressures from industry, Congress, the Presidential Administration and consumers. It should also feel pressures from practicing physicians and scientists.

In order to become more involved in these stages of the drug regulatory process, nongovernment physicians and scientists should begin to exercise their influence through their respective professional organizations, state and national medical societies, and specialty groups. Logically, a letter from these organizations representing a collective opinion has far greater weight in the regulatory process than individual letters. If the Food and Drug Administration receives opinions from these organizations early, before a regulation gets into the Federal Register, they are in a good position to respond with further study and review. Without such dissenting opinions, there is very little incentive to make changes in proposed regulations.

One instance in which practitioners did influence drug regulatory affairs in this way is the recent controversy that arose over the legitimacy of drug combinations. The strong opinion of practitioners on the value of such medication in clinical practice played a very prominent role in making the Food and Drug Administration modify its rather restrictive policy.

Another way in which practitioners can effectively influence drug regulations is by working with drug manufacturers conducting clinical trials of chemotherapeutic agents. When a drug is rated other than effective it may only mean that there is a lack of controlled clinical evidence as to efficacy. Thus, physicians might offer to conduct clinical studies that could help keep a truly effective drug in the marketplace. The treatment of diseases such as diabetes and angina are areas where the practitioner can aid in clinical studies because patients suffering from these diseases are rarely found in the conventional hospital setting.

By working with ethically and scientifically sound study designs in his everyday practice, the practitioner could begin to play an important part in determining official ratings on drug efficacy.

Nongovernment physicians and scientists and the FDA should also improve their lines of communication to the public. The medical community must develop a voice every bit as loud as that of the consumerists, the press, and others who sometimes criticize without complete information. If not, much of what the medical community *and* federal regulators do will often be represented in simplistic and somewhat misleading terms.

One illustration of the misuse of the media in this regard is the recall of anticoagulant drugs several years ago. This FDA action was given publicity by the press and television that went far beyond its probable importance. The result was a very uncomfortable situation for the practitioner who had patients taking these medications. Since the practitioner and pharmacist had not been informed of the action by the time it was publicized, in most states they were deluged with calls from worried patients.

The practitioner can attempt to solve these problems of inadequate communication in several ways. One would be the creation of a communications line in state pharmacy societies. When drug regulation news is to be announced, the society could immediately distribute a message to every pharmacist in the state. The pharmacist, in turn, could notify the physicians in his local community so that he and the physician could be prepared to answer inquiries from patients. Another approach would be to use professional publications the practitioner receives.

All of this leads back to my opening contention: if drug regulation is to be effective, timely, and related to the realities of clinical practice, a better method of communication and feedback must be developed between the nongovernmental medical and scientific communities and the regulatory agency.

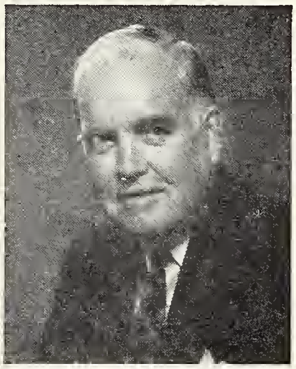
Advertisement

One of a series

ue

Maker of Medicine

Henry W. Gadsden,
Chairman & Chief Executive Officer, Merck & Co., Inc.



In my opinion, it is the responsibility of all physicians and medical scientists to take whatever steps they think are desirable in a law- and regulation-making process that can have far-reaching impact on the practice of medicine. Yet many events in the recent past indicate that this is not happening. For example, it is apparent from drug efficacy studies that the NAS/NRC panels gave little consideration to the evidence that could have been provided by practicing physicians.

There are several current developments that should increase the concern of practicing physicians about drug regulatory affairs. One is the proliferation of malpractice claims and litigation. Another is the effort by government to establish the relative efficacy of drugs. This implies that if a physician prescribes a drug other than the "established" drug of choice, he may be accused of practicing something less than first-class medicine. It would come perilously close to federal direction of how medicine should be practiced.

In order to minimize this kind of arbitrary federal action, a way must be found to give practitioners both voice and representation in government affairs. Government must be caused to recognize the essentiality of seeking their views. One of the difficulties today, however, is that there is no way for concerned practitioners to participate in the early stages of decision-making processes. They usually don't hear about regulations until a proposal appears in the Federal Register, if then. By that time a lot of concrete has been poured, and a lot of boots are in the concrete.

Physicians in private practice, and particularly clinicians, should press for representation on the advisory committees of the Food and Drug Administration, joining with academic and teaching hospital physicians and scientists who are already serving. Though practitioners may not have access to all available information, the value of their clinical experience should be recognized. Clinicians, for example, rightly remind us that difficulty in *proving* precise effects does not necessarily mean a drug is ineffective.

Unless practitioners are more involved in drug regulations, it will be increasingly difficult for the pharmaceutical industry and scientists elsewhere to make optimal progress in drug development. The benefit/risk ratio must be re-emphasized, and as part of this it must be acknowledged that benefit can come from the judgments of medical science as a whole. Even this concept, unfortunately, is not always accepted in drug regulatory processes. For example, if current medical opinion holds that an excess of total lipids and cholesterol in the blood is probably predisposing to atherosclerosis, and if a drug is discovered which reduces total lipids and cholesterol, the drug ought to be accepted *prima facie* as a contribution to medical science . . . until someone disproves the theory. The sponsor should not have to prove the theory as well as to develop and test the drug.

I feel a major new effort must also be made to erase the feeling of mistrust of medicine and of medicines that seems to be growing in the public consciousness. Triggered primarily by strident announcements in Washington, people are reading and hearing confidence-shaking things almost continuously. Although challenge and awareness are essential to medical advancement, our long-term goal is constructively to build, not destroy. This means strengthening patient-physician relationships based on mutual confidence and trust. And in matters of health policy, it means working toward participatory rather than adversary proceedings—where everyone with an interest and a capacity to contribute has an opportunity to be heard . . . and, if that opportunity is not spontaneously afforded him, he may seek it.

Opinion & Dialogue

What is your opinion, doctor?
We would welcome your comments.

P·M·A

The Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W., Washington, D.C. 20005

Request—Representative to CHL "Task Force on Smoking and Health"

A request was received from the chairman of this Connecticut Health League Task Force that the Council designate a representative to serve as a member of same. Being apprised that Marvin P. Zimmerman, Branford, has a special interest in this subject and has indicated a willingness to serve, the Council VOTED to request Dr. Zimmerman to accept appointment as a CSMS-designated member of the CHL Task Force on Smoking and Health.

Report—Committee to Study Perinatal Morbidity and Mortality

It was VOTED to receive for filing a report submitted by the Committee which recommended approval of a policy statement on routine serological testing as follows:

> "In addition to the initial prenatal serological test (for syphilis) required by law, all expectant mothers, on being admitted to a hospital for delivery, should have blood drawn for serology (VDRL)."

It was further VOTED to approve the foregoing policy statement and to implement the Committee's recommendation that it be publicized in an early issue of the Journal, and that notice thereof be made directly to hospital chiefs of obstetrics, hospital chiefs of pediatrics, the Connecticut Society of American Board Obstetricians and Gynecologists, the Maternal and Child Health Section of the State Health Department and the Commissioner of Health of Connecticut.

Request for Authorization—Section of Forensic Medicine

Having received an application from a group of interested members for authorization to form a CSMS Section on Forensic Medicine, and having been assured that the application and attachments complied with the pertinent provisions of the By-laws, the Council VOTED to approve the application and to transmit it to the House of Delegates on April 25 with the Council's recommendation that authorization be granted to the applicants to form such a section.

Request for Position Support—Section on Ophthalmology

It was VOTED to receive for filing a communication received from the president of the CSMS Section on Ophthalmology which requested Council support for the position of the Section that a second eye bank is not needed in Connecticut, and, if established, would have adverse effects on the existing eye bank at the New Britain Hospital because of conflicting jurisdictions, competition, etc. In addition, Dr. Taylor points out that the existing eye bank has proven itself capable of supplying all the clinical material needed in Connecticut as well as ample material for research purposes to the Yale Medical School; also, that substantial costs of setting up a second eye bank that is not needed would be wasteful of funds and personnel.

After considering the merits of the arguments presented by the Section, the Council VOTED to approve a statement as follows:

> "On the basis of available information at hand, the Council of the Connecticut State Medical Society does not approve of the establishment of a second eye bank in Connecticut and urges the Connecticut Hospital Planning Committee to make a critical evaluation of the proposal of the Yale Medical School to establish such a second eye bank."

It was further VOTED to send notice of this action to the Executive Director of the South-Central Comprehensive Health Planning Agency as information and for whatever action may be deemed appropriate.

Reconsideration of Action on Report of Committee on Statewide Medical Planning

At the Council meeting of March 22, 1972, the Council voted to receive for filing a report submitted by the Committee on Statewide Medical Planning on a proposed study to be made of ambulatory care in Connecticut; to approve in principle the proposed plan for the study as outlined in the report of the Committee; and to transmit the report to the House of Delegates on April 25 with the Council's recommendation that the House take similar action; i.e., to approve in principle the plan for the subject study outlined in the Committee's report.

Prefaced by an expression of opinion that the Council had taken the March 22 action on the basis of general and fragmentary information about the proposed study, furnished by the Committee's report, and that much more detailed and specific information was now available for study, a motion was made that the Council reconsider its subject action of March 22. After extended discussion, it was VOTED to reconsider the subject action.

Debating an ensuing motion to rescind the March 22 action ("approve the study in principle"), the members heard arguments, pro and con, about the relevance and/or importance of "detailed information" vs. "general information" regarding the proposed study to the "in principle" action under discussion. Subsequently, by show of hands, the motion to rescind failed to carry.

Thereafter, the Council took the following actions:

(a) It was VOTED to express confidence in the members of the Committee on Statewide Medical Planning with respect to their efforts to develop the proposed ambulatory care study.

(b) It was VOTED to direct the Committee on Statewide Medical Planning to prepare and present to the House of Delegates on April 25 a supplementary report (to the one received by the Council) which will embody all pertinent information concerned with the details of the proposed study that is available up to that time, in order that the House may consider this supplementary report and information in conjunction with the subject report and recommendation of the Council.

Expression of Appreciation to the President

A standing VOTE of appreciation was given to Frederick C. Weber, Jr., incumbent President of the Society, for the excellence of his performance in office and the dedication and initiative he has demonstrated in discharging his duties and responsibilities.

Acknowledgments

Noting that this was the final Council meeting for 1971-72, the Chairman, Kenneth F. Brandon, thanked the members for their cooperation and their sustained good nature during characteristically long and trying sessions. In response, the members gave the Chairman an appreciative round of applause.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on April 5, 1972. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by an interested member of the Society.*

Welcome, New Members

New Haven County

Gerald Gregory Anderson, M.D., 333 Cedar Street, New Haven, Connecticut.

John W. Brackett, Jr., M.D., Saint Mary's Hospital, Waterbury, Connecticut. . .

John L. Cornog, Jr., M.D., 310 Cedar Street, New Haven, Connecticut

Robert W. Ferraro, M.D., 636 Plank Road East, Waterbury, Connecticut

Gerald H. Flamm, M.D., 1450 Chapel Street, New Haven, Connecticut

John Dexter Forbes, M.D., Hinman Lane, Southbury, Connecticut

Richard Hemenway Dyer, Jr., M.D., 1211 West Main Street, Waterbury, Connecticut

Robert Humphries, M.D., Griffin Hospital, Derby, Connecticut.

Morris D. Kerstein, M.D., V.A. Hospital, West Haven, Connecticut.

Enrico G. Khu, M.D., 9 Roger Road, New Haven, Connecticut.

Thomas J. Krizek, M.D., 333 Cedar Street, New Haven, Connecticut.

Bernard J. Langenauer, M.D., 35 Lincoln Street, Hamden, Connecticut.

Robert Aaron Levine, M.D., 960 Main Street, Branford, Connecticut.

Dorothy Otnow Lewis, M.D., 309 Edwards Street, New Haven, Connecticut.

Robert B. Litman, M.D., 811 Orange Street, New Haven, Connecticut.

Douglas William MacRae, M.D., 477 South Broad Street, Meriden, Connecticut

Peter R. Manes, M.D., 1039 Chase Parkway, Waterbury, Connecticut.

Harley B. Meia, M.D., 122 Broad Street, Milford, Connecticut.

William B. McCullough, M.D., 2 Church Street South, New Haven, Connecticut.

Terence O'Callaghan, M.D., Saint Raphael's Hospital, New Haven, Connecticut.

Howard T. Robinson, M.D., Yale-New Haven Hospital, New Haven, Connecticut.

Marc A. Rubenstein, M.D., 255 Bradley Street, New Haven, Connecticut.

Jesse David Samuels, M.D., 314 Elizabeth Street, Derby, Connecticut.

Robert L. Scheig, M.D., Yale Medical School, 333 Cedar Street, New Haven, Connecticut.

Carl P. Sherwin, Jr., M.D., 377 Broad Street, Meriden, Connecticut.

Nira Rubin Silverman, M.D., 2 Church Street South, New Haven, Connecticut.

George J. Watstein, M.D., 2 Church Street South, New Haven, Connecticut.

Windham County

Edward R. Browne, M.D., Windham Community Hospital, Willimantic, Conn. 06226.

Stephen R. Perry, M.D., Box 10, Mechanicsville, Conn. 06252.

Perry G. Rawson, M.D., Day-Kimball Hospital, Putnam, Conn. 06260.

Placement Opportunities

Allergist—Wanted as soon as possible. Must be board eligible for a two-man allergy practice which now requires a third man. Work week is four days; every third weekend off. Early partnership for right man guaranteed. 100,00 population. Centrally located in a university town. Connecticut license required. First year-five figure salary. Area Code 203 346-1575.

Allergist—Wanted as soon as possible. To join allergy practice in the southern part of the state. Large shore community.

Allergist—Opportunity in medium size community in Fairfield County. Convenient to New York

Anesthesiologist—Two board eligible or certified anesthesiologists needed in urban hospital in the central part of the state.

Anesthesiologist—Large urban hospital has vacancy. Located in western part of the state.

Anesthesiologist—To join three man group in 180 bed community hospital. Interest in inhalation therapy and respiratory physiology important. Recent or near future residency graduate acceptable. Living conditions excellent in semi-rural area with nearby University of Conn. and State College affording many recreational and cultural advantages. Please contact Anesthesia Associates, P.O. Box 23, Willimantic, Connecticut 06226. Tel. 423-9201.

Anesthesiologist—To join Board certified chief of anesthesiology in small community hospital. No OB. Salary negotiable. If interested contact administrator or chief of anesthesiology. Johnson Memorial Hospital, Stafford Springs, Connecticut 06076.

Anesthesiologist—Associate position in medium sized community. Centrally located.

Emergency Room Physician—To complete four-man group. 100-bed, full service hospital. Solid backup in all specialties and most subspecialties from Active Staff. Central Connecticut community midway between Hartford and New Haven. Must be eligible for Connecticut licensure. Attractive salary, excellent benefits. Resumé to Chief of Staff, World War II Memorial Hospital, Meriden, Connecticut 06450.

Family Practice—Two physicians seeking a third in attractive shore community. Busy summer practice. Hospital conveniently located. Send resume to Karl R. Friedman, M.D., Old Lyme, Connecticut 06371.

Family Practice—Practitioner needed in rural community in the western part of state. Physician in community willing to assist in establishing newcomer in rural, solo practice.

Family Practice—Suburb of New Haven has opportunity for an associate in family practice.

Family Practice—Physicians in community northwest of New Haven searching for additional practitioner. Small, up-to-date community hospital.

Family Practice—Practitioner wants to retire. Very attractive practice in southwestern Connecticut. Shore community. Near NYC.

Family Practice—Darien has ideal arrangement for newcomer. No OB. No surgery. Recently deceased physician had well established practice. Contact James V. MacGregor, M.D., 2 Queen Lane, Darien.

Family Practice—Two cities just north of Hartford in search for practitioners. Growing communities on Connecticut River. Physician Search Committees willing to assist newcomer with free office rent, etc.

Family Practice—North Branford, All America City, suburb of New Haven, requires family physician to establish practice. No other physician at this time. Contact Irving H. Beck, Town Manager.

Family Practice—Southwestern Litchfield County. Community hospital. Conveniently located. Community physicians also searching for pediatrician and Ob/Gyn to enter private practice.

Family Practice—Growing community seeks family physicians. North-central Connecticut. Approximately 47,000 population. Several hospitals in the area. New hospital in planning stages. Number of specialists in town. Conveniently located.

General Practice, Internal Medicine, Ob-Gyn and ENT: Needed in town of Torrington. 200 bed hospital. 50 physicians, over 50,000 population, Contact Joseph F. J. Curi, M.D., Chairman of Search Committee, Charlotte Hungerford Hospital, Torrington, Connecticut 06790. 203-482-0441.

General Practice and Internal Medicine—Both for solo and hospital based practice. Medium sized, north central community. Community hospital. Needed immediately.

General Medicine and Internal Medicine—Northwestern Connecticut community seeking to attract practitioners. Associate type practice possible.

Insurance Company Physicians—Three companies have vacancies. Internists, general practitioners, surgeons.

Internist—Community physicians seek additional internist to establish practice in medium size city northwest of New Haven.

Internist—Scenic northwestern community needs an internist. Physicians willing to assist candidate.

Internist—Interest in allergy, rheumatology or infectious diseases. Association with large clinic in central Connecticut.

Internist—Needed immediately to associate with large practice. Darien-Stamford area.

Internist—University setting. New facility. Ideal for proper candidate.

Internist—Northwest Connecticut prep school, good salary, excellent retirement benefits, family living, schools, recreation, large house, facilities for private patients, vacations. Help practice busy board certified FACP. 100 miles New York City, one hour Hartford, Albany. Curriculum vitae to: F. E. Smith, Jr., M.D., F.A.C.P. Salisbury, Connecticut 06068.

Internist—Rural community, but close enough for commute to Hartford. Small, community hospital. Physicians searching for additional coverage.

Internist—A third Internist is needed to join two other Internists in the town of Manchester, Connecticut. Office located across the street from a 300 bed community hospital which is currently in the second of a three stage building program. Manchester is located fifteen minutes from Hartford, one hour from New Haven, one hour and a half from Boston and two hours from New York City. For further information contact: Harold J. Lehmus, M.D., or David L. Warren, M.D., 56 Haynes Street, Manchester, Connecticut 06040. Telephone: 203-646-1167.

Internist—Preferably Board Certified or eligible, for chronic disease and cancer hospital having sections for TB in adults and children. 35 hr. week, 11 paid holidays, sick leave, 3 weeks vacation after one year of service. Salary level: $23,227-28,333. Paid health insurance and minimum charge for life insurance. Apartment available for physician with small family. Write Medical Director, Uncas-on-Thames Hospital, Norwich, Connecticut 06360.

Neurologist—Litchfield County area. Search Committee of the Medical Staff will assist qualified candidate.

Neurosurgeon—Opportunity in southwestern shore community. Near N.Y.C.

Ob/Gyn—Community in western Connecticut in search of physician to open private practice. Community's growth requires additional medical services.

Ob/Gyn—Associate needed. Attractive community. Short distance from Waterbury.

Ob/Gyn—Associate needed for Waterbury group.

Ob/Gyn—Fourth ob/gyn needed in southeastern Connecticut town.

Ophthalmologist—Three vacancies. Each in the larger cities of Connecticut. Immediate opportunities.

Ophthalmologist—Associate needed to join two other ophthalmologists in large, centrally located Connecticut city.

Otolaryngologist—Two physicians approaching retirement. Eastern part of the state. Coastal area.

Otolaryngologist—Central Litchfield County in search for specialist.

Pathologist—Needed to join staff of hospital in large southwestern shore community.

Pathologist—Chief of Pathology wanted for 100 bed, full service community hospital. Excellent lab facilities, well staffed and equipped. Fee for service or salary. Central Connecticut. 20 minutes to either Hartford or New Haven. Resumé to Chief of Staff, WW II Memorial Hospital, Meriden, Connecticut 06450.

Pediatrician—Community physicians feel that another pediatrician is needed. Central section of the state. 40% of population 18 years of age and under.

Pediatrician—currently board-eligible or board certified. Full-time position. Salary negotiable. To practice family oriented medicine in a private, non-profit neighborhood health center. For further information please contact Evans H. Daniels, Jr., M.D., Medical Director, Community Health Services, Inc., 1023 Albany Avenue, Hartford, Connecticut, 06112. Telephone 549-1423.

Pediatrician—Needed to join physician in the Waterbury area.

Pediatrician—Community of Enfield needs pediatrician. Growing community north of Hartford.

Pediatrician—To join pediatrician in northeastern portion of the state.

Proctology—Lucrative practice available in New Haven. Physician deceased. Fully equipped office. Contact: A. M. Murray 203-787-4161.

Psychiatrists—Needed for state facility. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

Psychiatrists—Openings in mental hospitals and mental health clinics under the auspices of the State of Connecticut. Write Personnel Administrator, Department of Mental Health, 90 Washington Street, Hartford.

Psychiatrist—Board Certified or Eligible, to Direct Mental Health Clinic in General Hospital, half time, $15,000 to $25,000 depending on qualifications, opportunity for private practice, prefer with clinical experience and interest in development of comprehensive community services; attractive living in semirural community with University, near urban centers; send curriculum vitae with inquiry to Richard B. Ogrean, Administrator, Windham Community Hospital, Willimantic, Connecticut.

Radiologist—Needed immediately at Veterans Hospital. Contact Medical Director, Rocky Hill Veterans Hospital, Rocky Hill, Connecticut.

Radiologist—Small community hospital in northwestern part of the state needs a radiologist.

Radiologist—Large hospital needs radiologist.

Senior Physician—positions available at Norwich Hospital. Primary responsibility for medical care of geriatric and mentally ill patients in a community oriented, geographically unitized hospital with many forward looking, exciting programs. Starting salary $20,465, many fringe benefits, housing available. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

Urologist—For association with well established practice in large, southwestern shore community.

General Surgery—Board certified surgeon seeking Board certified partner or associate in general surgery to practice in northern Connecticut. Small community hospital. Attractive community. Conveniently located. Write Physician Placement Service.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS' PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT

Placement Wanted

The Placement Service has numerous resumes on file for physicians available for positions in Connecticut. Space does not permit printing individual advertisements. Anyone interested in resumes of candidates in the following specialities are asked to contact the Placement Service for more information (865-0587): allergy, anesthesiology, dermatology, family practice, internal medicine, neurosurgery, ob/gyn, ophthalmology, orthopedics, otolarynology, pathology, pediatrics, psychiatry, radiology, surgery, and urology.

Allied Personnel

EEG Technologist—31 years of age. Nine years of experience. Wishes position as instructor in clinical EEG Technology or technologist in charge of new laboratory. Available June 1. Presently at University of Kentucky completing degree program. Richard F. Wilmarth, 133 Brown Avenue, Lexington, Kentucky 40505.

Physician's Assistant—30 years of age. Presently enrolled in Physician's Associate Program at Duke University. Available September 1972. Desires position with general practitioner, pediatrician or internist in solo or group practice. Ralph B. Lenoci, 261 King Street, Port Chester, New York 10573.

Business Manager—College graduate; 13 years administrative experience in clinic, hospital and health care fields. Available within 30 dasy. Irven V. Roberts, 85 Prescott Street, Torrington, Conn. 06790. 482-8398.

Physician's Associate—Special training in general surgery, urology, orthopedics and plastic surgery. Experience as a OR scrub technician. B.S. Degree. Will complete P.A. Program at Duke University in August. Patricia E. McNabb, 802 Louise Circle, Apt. 29-L, Durham, North Carolina 27705.
MEDIHC Program—Former military medics; number of candidates available. Contact: Henry J. Miller, Military Experience Directed into Health Careers, 640 Chapel Street, New Haven, Connecticut 06510. Phone: 865-0862 collect.

Summer Employment Wanted — Camp physicians; part time or vacation coverage. Medical students seeking hospital or laboratory positions. Contact: Connecticut State Medical Society—203-865-0587.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS' PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Meeting Notices

The information on this "notices" page is offered as a service of all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the month preceding date of issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

GENERAL

September, 1971—May, 1972
Lecture Series—Each Tuesday
Basic Sciences As Related to Clinical Medicine:
Infectious Diseases, Coronary Care Problems, Diagnosis and Treatment of Tumors
Lawrence and Memorial Hospitals
New London, Connecticut
Contact: Edward Gipstein, M.D.

June 1-3—Thursday-Saturday
National Conference on Cancer Chemotherapy
The Biltmore Hotel, New York City
Contact: American Cancer Society
219 East 42nd Street
New York, New York 10017

June 12-16—Monday-Friday
5th Conference on The Clinical Delineation of Birth Defects
Johns Hopkins Medical Institutions
Baltimore, Maryland 21205

CARDIOLOGY

June 8-11—Thursday-Sunday
Cardiac Arrhythmias
Virginia Beach, Virginia
Contact: Charles L. Baird, Jr., M.D.
Medical College of Virginia
Richmond, Virginia 23219

GASTROENTEROLOGY

June 8-10—Thursday-Saturday
Advances in Clinical Gastroenterology
Yale University School of Medicine
New Haven
Contact: Howard M. Spiro, M.D.

OCCUPATIONAL HEALTH

September 11-12—Monday-Tuesday
32nd Annual AMA Congress on Occupational Health
Drake Hotel, Chicago, Illinois

PEDIATRICS

June 6—Tuesday—6:30 P.M.
Spring Meeting of the Beardsley Chapter of the American Academy of Pediatrics
Speaker: Thomas Cone, M.D., Professor of Pediatrics, Children's Hospital, Boston
Hawthorne Inn, Berlin Turnpike

PULMONARY PHYSIOLOGY

October 22-25—Sunday-Wednesday
Clinical Pulmonary Physiology
Poughkeepsie, New York
Contact: New York Trudeau Society
Room 710, 105 East 22nd Street
New York, New York 10010

Electrocardiogram of the Month:

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

The Significance of QT, QTc, QaT, and QaTc: continued

I—Prolongation of QT interval with increase in QTc value—

It will be recalled that QT measures the duration of the whole period of ventricular repolarization and when corrected for heart rate is QTc. Normally the value of QTc is in the range of 0.38 to 0.42. When the terminal phase of repolarization is prolonged the QTc value exceeds 0.42. This occurs in a variety of primary cardiac diseases, in diseases of the central nervous system, in association with electrolyte abnormalities, and following intake of certain drugs.

Fig. 1 A is the electrocardiogram of a male, age 60, taken during the course of a routine physical examination. The QTc value is normal at 0.38. Fig. 1 B is the tracing of the same patient taken several days after onset of infarction of the anterior wall. Note that the T waves are now wide and deeply inverted in leads I, aVL, and the chest leads. The interval between Q and the onset of the T wave (QaT) is not prolonged. However, the QT interval measures 0.36 second and the QTc value is increased to 0.45.

Fig. 2 A shows the effect of Quinidine upon the duration of ventricular repolarization. The serum level of Quinidine was 8.2 mgm./Liter. The QT interval measures 0.56 second. The QTc value is increased to 0.53. Note that the prolongation of the QT interval is due mainly to marked widening of the T wave. Fig. 2 B was obtained several days after withdrawing Quinidine. Note the significant decrease in the width of the T wave. The QT interval now measures 0.44 second and the QTc value has decreased to 0.43.

II—Prolongation of QaT interval with increase in QaTc value—

It will be recalled that QaT measures the time in seconds from Q to the apex of the T wave and represents the initial slow phase of ventricular repolarization. Corrected for heart rate it is termed QaTc. Normally the value of QaTc is in the range of 0.28 to 0.32. Prolongation of QaTc is most commonly observed in disease states in which the serum level of ionizable calcium is reduced. Less common states in which the QaTc value is increased are hypothermia and certain rare hereditary disorders. Fig. 3 A shows the effect of hypocalcemia upon the ventricular repolarization time in a patient whose serum calcium level was reduced to 6.2 M.eq./Liter due to hypoparathyroidism. Note that there is a long isoelectric ST segment with delay in onset of the T wave. The QaT interval measures 0.36 second. The QaTc value is increased to 0.42.

Fig. 3 B taken 3 months later after the calcium level had been restored to 9.4 M.eq./Liter by administering calcium and dihydrotachysterol exhibits a QaT interval of 0.30 second and the QaTc value is now normal at 0.33.

(To be continued)

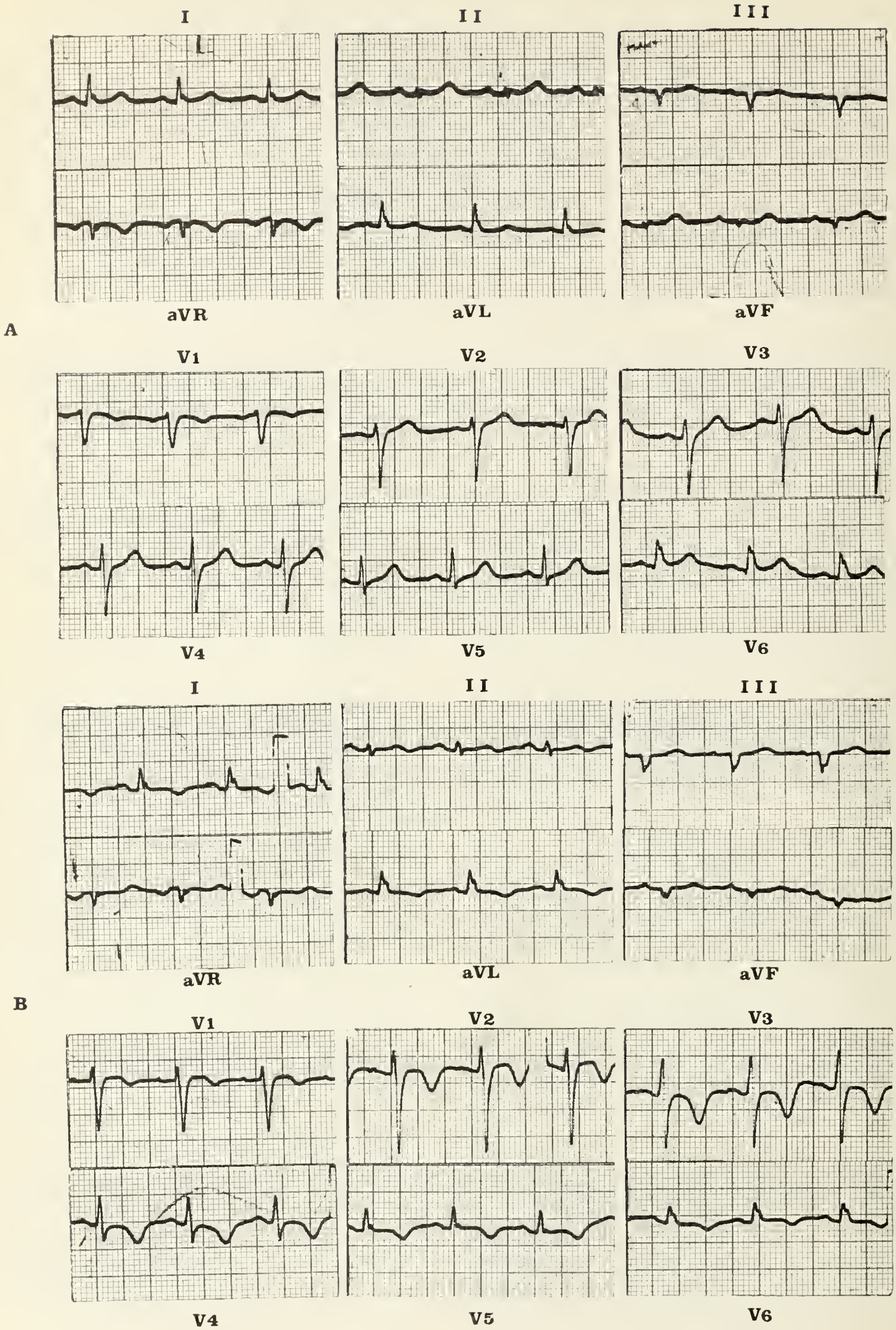

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Figure 1

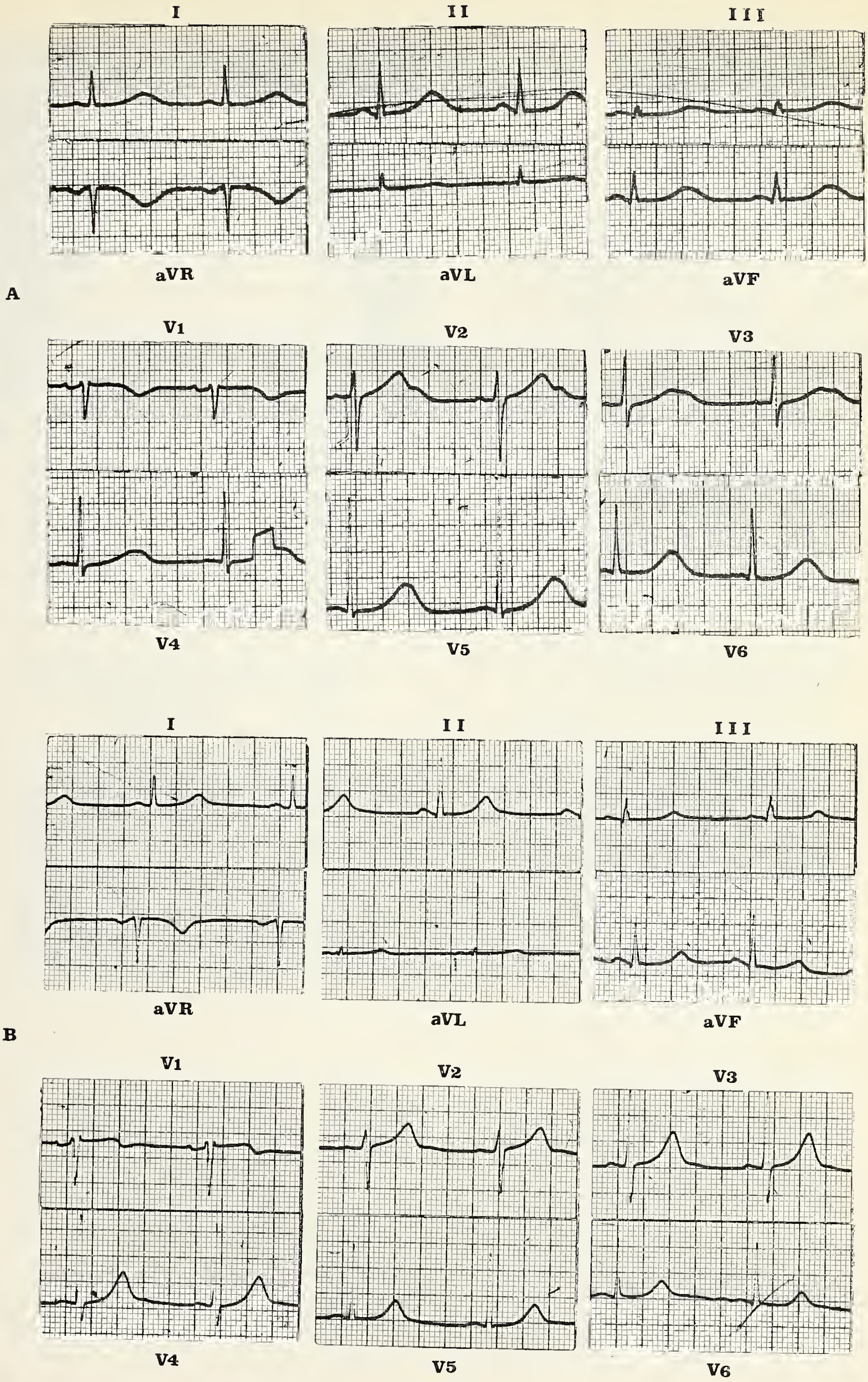
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Figure 2

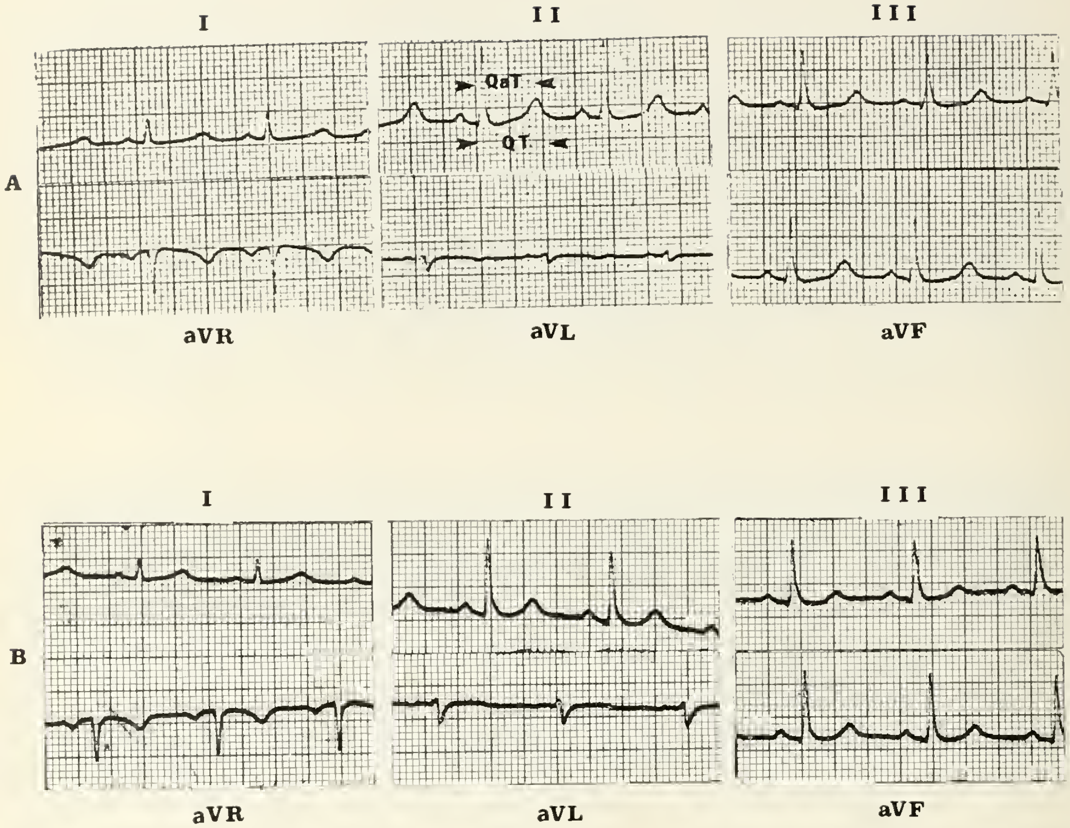

Figure 3

np

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New Lakeview Convalescent Home

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A Psychiatric Unit for the short term patient has opened at New Lakeview Convalescent Home, an ECF in Cheshire. Staff and consulting psychiatrists work with specialized staff members to provide highly individualized treatment programs—the rates for this service are set at a moderate level for the patient. Medical problems are under the direction of a physician devoting time exclusively to this 30 bed unit. The Home is accredited by the joint commission on accreditation of hospitals. New Lakeview a 210 bed facility, is set in the country overlooking a lake and is located at 50 Hazel Drive, Cheshire. Further information can be obtained from Mr. Stephen Potash, Administrator, at 272-7204.

OBITUARIES

Ettore Francis Carniglia, M.D.
1904-1971

Dr. Ettore Francis Carniglia, age 67, of 5 North Main Street, Windsor Locks, Connecticut died October 23, 1971 at his home. He was a lifelong resident of Windsor Locks, having practiced there for 38 years. He graduated first in the Class of 1921 of Loomis School, Windsor, and in 1925 he received his A.B. degree from Harvard magna cum laude. In 1929 he graduated from Harvard Medical College with an M.D. degree and was a member of AOA, the honorary medical fraternity.

He interned at Hartford Hospital in 1931 and at the Union Memorial Hospital (a division of Johns Hopkins Hospital in Baltimore, Maryland) in 1932.

He began his medical practice in Windsor Locks in 1933. He was made town health officer in 1934 and served in that capacity until September of 1960, when he resigned. During his years as town health officer, Dr. Carniglia also served on a number of town boards, including the Board of Education. He also served at one time as chief of the visiting staff at the Hartford Hospital. He was a Fellow of the American Medical Association, a member of the Connecticut State Medical Society, and the Hartford County Medical Association.

Dr. Carniglia was a communicant of St. Mary's Church and was a fourth degree member of the Knights of Columbus. He was also an honorary member of the Windsor Locks Rotary Club and an honorary citizen of Boystown, as well as being a director of the Windsor Locks Savings and Loan Association for many years.

He leaves his wife, Mrs. Blanche Goodsell Carniglia, his son, Peter M. Carniglia of Windsor Locks, and a daughter, Mrs. Margaret Malec of Windsor Locks, a brother, Francis J. Carniglia of Windsor Locks, and six grandchildren.

Dr. Carniglia was a most unique person in many respects. He graduated from Harvard College in a brilliant class, including the controversial physicist, Julius Oppenheimer of atom bomb fame, and Dr. Carniglia was somewhat upset when Oppenheimer was criticized for disloyalty as Dr. Carniglia had utmost confidence in Oppenheimer's integrity, and time has taken care of that confidence.

Dr. Carniglia could easily have gone, and was requested to go, into the academic phase of medicine where he would have served with distinction, but for reasons of his own he chose to return to his own environment and the people he loved. He made no mistake. He became the epitome of "the beloved physician" of central Connecticut and without question was the "Sir William Osler" of his generation. He was a most astute observer and diagnostician and never hesitated to ask for advice when needed. When "Carny", as he was affectionately known by his colleagues and patients, asked for advice one knew they were confronted with a problem.

He was a most gifted teacher to the interns and residents of the Hartford Hospital and could hold his head high in any medical meeting.

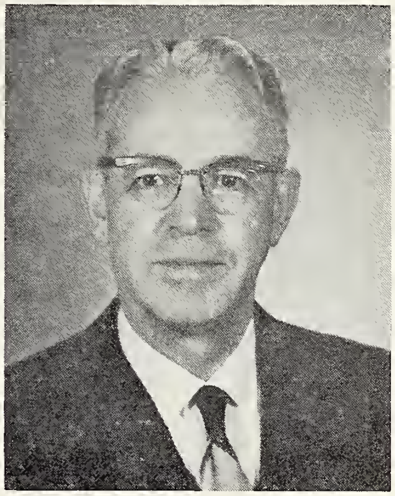
Dr. Carniglia was most astute when he married Miss Blanche Goodsell, the former obstetrical supervisor at the Hartford Hospital. She, as not many young women would have done, fitted into his way of life and became his "right hand". They had office hours 24 hours a day and no person was turned away or refused advice and care. They were able to handle quality and quantity. It has been a privilege to have known Dr. Carniglia, and it will be one of the staff's cherished memories at the Hartford Hospital to have known and worked with him. Congresswoman the Hon. Ella T. Grasso of the Sixth Congressional District read into the Congressional Record on October 28, 1971 a beautiful tribute to him entitled "The Whole Town Mourns".

Frank O. Wood, M.D.

Louis E. Garston, M.D.
1903-1972

Louis E. Garson, M.D. of Torrington, a leading dermatologist in the State, died at St. Mary's Hospital, Waterbury, on March 25, 1972. He was 69 years of age.

He started in General Practice in Torrington at about the same time as I did. Throughout the ensuing years a deep and abiding friendship existed between us and our respective families.



Lou was born in Russia, and migrated to New Haven during early childhood. He graduated from the local schools there and attended Yale University and graduated from the St. Louis University School of Medicine.

He interned at the Grace New Haven Hospital, and served his residency at Mt. Sinai Hospital in Hartford. Before entering private practice he served as a First Lieutenant in the Medical Corps of the U.S. Army.

After several years of General Practice in Torrington he did post-graduate work at the Skin and Cancer Hospital in New York City; following which he specialized in the practice of Dermatology.

In June of 1953, his article on "Drug and Chemical Sensitization" appeared in the *Connecticut State Medical Journal*, abstracts of which were subsequently written up in other leading Journals.

He was a Senior Attending Physician and Chief of Dermatology at the Charlotte Hungerford Hospital. Lou was a Past President of the following organizations: the Litchfield County Medical Society, the Torrington Medical Society, the Dermatology section of the Connecticut State Medical Society and the Beth El Synagogue in Torrington. A leader in the local religious community, he served on the Board of Directors of the Beth El Synagogue from 1945 to 1952.

Dr. Garston was a member of the New England Dermatological Society; the American Academy of Dermatology; the American Society of Dermatological Surgery; and a member and Past Chairman of the Physicians and Pharmacists Committee of the Connecticut State Medical Society.

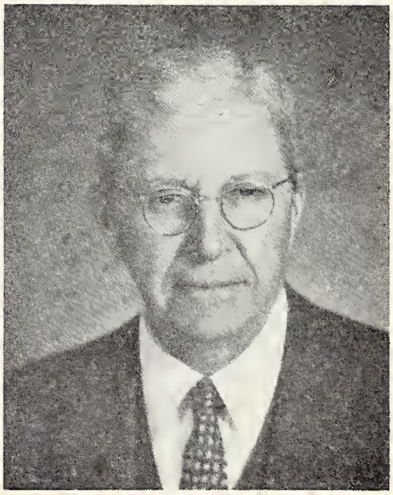
He was also a member of Temple Beth Israel of West Hartford and its Men's Club; Seneca Lodge No. 55, A. F. & A. M.; the B'nai B'rith Lodge, both of Torrington and the Litchfield County University Club.

Dr. Garston is survived by his wife Lenola Antupit Garston; a son Michael of New York City; three brothers, Leonard of Milford, Alfred of Waterbury and Benjamin of West Hartford, and a sister, Mrs. Nora Morris of New Haven. Funeral services were held at the Weinstein mortuary West Hartford, March 26, 1972 with Rabbis Abraham Feldman and Harold S. Silver officiating. In his most impressive eulogy on Lou, Rabbi Silver described him aptly as the Patriarch of his family. In my humble opinion, I feel that we, the Litchfield County Medical Society have lost both a Patriarch and a Sage.

I. S. Goldberg, M.D.

Brae Rafferty, M.D.
1901-1972

Dr. Brae Rafferty was born in Willimantic, Connecticut, September 6, 1901, son of Frank and Mary Rafferty. He graduated from Brown University in 1924 and from Jefferson Medical School in 1928, interning at Mercy Hospital in Altoona, Pennsylvania.



Dr. Rafferty returned to Willimantic and entered into the practice of medicine in 1933 and was a member of the surgical staff until his retirement in 1968.

Dr. Rafferty was a fine gentleman and physician who served his patients to the full limit of his abilities. He was a forceful and direct man of good judgment. He was a man of many interests—an antiquarian—historian, long organizer and president of the Windham Historical Society, making himself an authority on local history.

Dr. Rafferty served his hospital and community well. He occupied various positions in the state including chief of surgery and president of the medical staff of the Windham Community Memorial Hospital. Dr. Rafferty was president of the Windham County Medical Association in 1937, and president of the Connecticut State Medical Society in 1951. He was a member of the Windham County Medical Association, the Connecticut State Medical Society, and the American Medical Association.

He was medical examiner for the Town of Windham for many years and an important leader in the development of medical examiner and toxicology services for the State of Connecticut. His medical examiner reports were not only models of accuracy but were written in a literary style that made them unique.

Besides his wife Ann, he is survived by two sons, Brae Jr., and Frank Patrick, and one daughter Madge Rafferty.

Edwin H. Basen, M.D.

In Memoriam

Balsam, Alan, University of Pennsylvania, 1958. Dr. Balsam was a practicing psychiatrist in the New Haven area since 1958. He was a member of the American Psychiatric Association and also a member of the New Haven County Medical Association and the Connecticut State Medical Society. Dr. Balsam died March 25, 1972, at the age of 44.

Caplan, Henry, Yale Medical School, 1927. Dr. Caplan was a practicing cardiologist in the New Haven area until his retirement in 1963. From 1943 to 1946, he was a captain in the U.S. Medical Corps. He served as president of the New Haven County Medical Association in 1964 and also held positions at Memorial Hospital, Bradley Memorial Hospital, and Meriden-Wallingford Hospitals. Dr. Caplan was a member of the New Haven County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Caplan died March 1, 1972, in Miami, Florida, at the age of 72.

de la Vergne, Paul Mason, McGill University School of Medicine, 1935. He was a former superintendent of Undercliff State Hospital and a consultant at Meriden Hospital, and served as secretary to the Meriden-Wallingford Hospital Board of Directors. He was a member of the New Haven County Medical Association and the Connecticut State Medical Society. He died March 22, 1972, at the age of 63.

Irving, J. Grant, University of Toronto Medical School, 1932. Dr. Irving was made a Fellow of the Royal College of Surgeons, Edinburgh, in 1934, and came to Hartford in 1935. In World War II, he attained the rank of Major as a neurosurgeon in the U.S. Army Medical Corps, serving in the U.S.A., Britain, and Western Europe. At his death, he was President of the Hartford Medical Society, Chairman of the Hartford County Medical Foundation, a Director of the Connecticut Diabetes Association and of the Greater Hartford Council on Alcoholism, and Chief Medical Director of the Aetna Life and Casualty Company. Dr. Irving died at the Hartford Hospital, March 11, 1972, at the age of 64.

Rafiee, Ali Akbar, Tehran Medical School, 1945. Dr. Rafiee was a practicing otolaryngologist in the Hartford area since 1959. He was a member of the Board of Otolaryngology and on the staff of New Britain General Hospital. Dr. Rafiee was a member of the Hartford County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Rafiee died March 8, 1972, at the age of 50.

Doctors And Overpopulation

(*Lancet* 1:374, February 12, 1972, Rea., J. N.) Ann Cartwright's much quoted 15% of births whose mothers were "sorry it had happened at all" did not change between 1968-1970. Dispite the introduction of the abortion act. The ill effects on the child of having been unwanted in infancy are difficult to assess but they are likely to be important and damaging to the development of personality.

The recent study of Crellin, et al, on the fate of the illegitimate children born in the first week of March 1958 throws some light on this question. —L.H.N.

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NUTRITION AND THE AUXILIARY

The Women's Auxiliary to the Connecticut State Medical Society has from its beginning recognized the importance of good nutrition as the basis of good health. Two nutritionists, former American Dietetic Association members, were among the physicians wives who organized the Auxiliary and later because presidents of this, our organization. Not only were they leaders of the Connecticut Auxiliary, but they also held positions, from time to time, on the Regional and National Auxiliary Boards.

Because of their knowledge of nutrition and health, they early encouraged the Auxiliary to become a member of, and support, the workings of the Connecticut Nutrition Council. The aim of the Council has been to disseminate nutrition information to the people of the State in the form of workshops for women, especially in deprived areas. They actually provided low-cost menus to families in need of such information. One of these nutritionists (a doctor's wife, of course) was for years an active member and officer of the Nutrition Council. It was this same Council, together with other community agencies, that organized "Meals on Wheels". Many communities in Connecticut have our members actively working on this program at the present time.

When our Medical Society was ready to organize the Connecticut Advisory School Health Council in 1954, it asked the Auxiliary to become an active participant. One of these same nutritionists was the original By-Laws chairman of the organization. Later, she became its president, and still remains our active representative. Today she is a working member of the subcommittee whose function is to draw up a "position paper" for the Commissioners of Education, of Health, and of Mental Health on the Nutritional Practices of the Lunch Program in our Connecticut schools. The Connecticut Advisory School Health Council has worked to upgrade the education of teachers and the curriculum for students in healthful living, which of course, at its root stresses the need for proper nutrition.

Our State Auxiliary and two of our County Auxiliaries have in the past provided scholarships to teachers enrolled in summer programs which aim at instructing the teacher-student in healthful patterns of family living. This instruction also included the value of good nutrition.

The speaker for our semi-annual meeting this year was Dr. Sarah Hunt, Assistant Professor of Nutrition at the University of Connecticut Medical and Dental School. Our women were especially enticed by her explanations of many new food fads and diets that are currently popular.

Thus, working actively with, and through other State organizations, we feel that our Auxiliary has been a catalyst in bringing the knowledge and the need for proper nutrition as the basic ingredient of good health to all citizens of Connecticut. We know that our new National President, Mrs. Robert F. Beckley, is a nutritionist and we are looking forward to any new programs she may initiate or implement this next year. As a home economist, she realizes that nutrition—proper diet—is a very real problem in our land of plenty as well as the underdeveloped, Third World countries.

Mrs. Dewey Katz
Chairman—Community Health
and Children and Youth
Committees

AMERICAN MEDICAL POLITICAL ACTION COMMITTEE CONNECTICUT MEDICAL POLITICAL ACTION COMMITTEE WHAT ARE THEY AND WHY ARE THEY?

AMPAC and COMPAC are political action committees within the framework of medicine.

AMPAC represents national medical political action and part of its function is to be continually knowledgeable about the political atmosphere in Washington as it relates to medicine, the physician, his patients, and his family. By so doing, AMPAC is equipped to advise the various state medical political action committees (PACS) and give them assistance when needed, fulfilling its political role through volunteers and trained personnel. AMPAC is the political arm of medicine.

COMPAC is Connecticut's Medical Political Action Committee which attempts to fill a role similar to AMPAC, but is concerned with the political problems related to medicine in the State. The State medical political activity is performed by two different committees. One of these committees is called COMPAC and the other is called the Public Affairs Committee of the C.S.M.S. The purpose of the Public Affairs Committee is to encourage participation in political action, to provide political education to the membership, and to promote membership in COMPAC. The purpose of COMPAC is to encourage individuals to become candidates for political office and to help candidates get elected. COMPAC has always interviewed potential candidates for public office in the State and will continue to do so and will carefully screen and support candidates who share the viewpoint of organized medicine and are sincerely concerned with the health of the public.

To perform their functions effectively both COMPAC and AMPAC need money more than anything else and the chief source of money is the annual dues and contributions of physicians and their wives. COMPAC dues for physician's wives are $10.00 per year and for both COMPAC and AMPAC the dues are only $20.00 per year—a tiny investment to help create the impressive potential impact of a strong political action committee. In addition to money, each of us can devote some time and energy to work for our favorite party or candidate. Let's go all the way and volunteer our help.

The physicians serving on both COMPAC and the Public Affairs Committee of the Connecticut State Medical Society are hard-working, dedicated men who devote much effort and would be encouraged to know that the women are behind them wholeheartedly.

Organized medicine realizes that it is far behind other organized groups in political action and its effectiveness has suffered because of this. Now medicine has to work doubly hard in the immediate future to maintain freedom for medicine in this country. This 1972 is a crucial election year and time is fast slipping away. Let's keep the faith; don't wait; join today. Remember that our elected politicians will be making the laws that regulate our lives.

Send dues and contributions to:

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Prophylactic Portocaval Anastomosis

(*Medicine* 51:27, 1972). Professor Harold O. Conn and his associates at Yale report on the results achieved in portocaval anastomosis in 68 cirrhotic patients with esophageal varices and bleeding over a 12 year period. They concluded that the operation does not prolong life. They believe that the operation which has been employed routinely for 24 years will probably be abandoned. —L.H.N.

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Better Rhubarb

(*Nature* 235:307, February 11, 1972). Not only animals are infected with viruses but plants and vegetables are also. For example, rhubarb (rheum rhaponticum) has been found to be widely infected with viruses including turnip mosaic virus, cherry leaf role virus and strawberry latent ringspot virus.

Apparently they do not cause visible symptoms or distress in rhubarb but they do affect the overall vigor of the infected plant and prevent them from giving their full potential yield of marketable material.

It has now been shown that infected rhubarb produce only half a plant size as compared to a noninfected stock. When leaves and leaf stem were harvested from virus free plants the virus free plant gave 101 percent greater weight petioles per plant than did the corresponding infected plants. The difference was easy to see for virus free plants were quite obviously larger and more vigorous at the end of the trial.

At least one vegetable has been transformed to double its yield by freeing it from virus infection. The implication of this finding for agriculture is beyond imagination.—L.H.N.

Cigarette Smoke Contributes Much Cadmium To The Body

(*Lancet* I:291, February 5, 1972, Lewis, G. P., et al.) Cadmium, a nonessential potentially toxic metal accumulates in human tissue with advancing age. Because many foods contain cadmium, the diet has been considered the major source for man.

Cigarette tobacco contains appreciable amounts of Cadmium which on burning passes into the smoke. Analysis of necropsy material has shown that nonsmokers accumulate smaller amounts of cadmium in their organs than smokers.

In addition, the accumulation in smokers is related to the numbers of pack-years smoked. The authors conclude that smoking constitutes a major source for cadmium accumulation in man.—L.H.N.

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Indications

Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (i.e. several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications

Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings

When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with the high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children Not recommended for use in children under 12 years of age.

Precautions

In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorectic agent and a restrictive dietary regimen.

Adverse Reactions

Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration

The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage

Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

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NEW BOOKS IN REVIEW

DOCTOR AND PATIENT AND THE LAW. R. Crawford Morris. Esq. and Alan R. Moritz. M.D. Fifth Edition The C. V. Mosby Co. St. Louis, 1971, pp 554. $24.50

Reviewed by: J. ALFRED FABRO

The medical profession is presented with another book on medico-legal problems to add to the long and growing list. But this is among the best. The fact that it is a fifth edition, originally published by deceased Louis J. Regan, M.D., LL.B., is evidence enough of its excellence and acceptance by the profession.

Mr. Morris and Dr. Moritz are also experts in the field. If there is one book a practicing physician should want in his own library covering the broad field of all legal aspects related to the practice of medicine, I would recommend this one without hesitation.

It deals not only with that area that haunts physicians more all the time—malpractice, but with all legal aspects related to medical practice.

The subjects are too numerous to enumerate, but they can be classified under a few general headings as outlined by the authors: (1) rights and duties of physicians, (2) rights and responsibilities—patients and physicians, (3) medical testimony (4) professional liability, and several nonrelated subjects in an appendix, such as a professional liability prevention program, and a model constitution for a medical society.

Under rights and duties of physicians, they discuss in detail sufficiently and clearly for physicians the history of requirements for licensure and the legal relation of physicians to hospitals and to medical societies.

Fees are discussed in one chapter. Most physicians, without having explored the subject, might think that there is no problem to discuss about fees. But after reading this, he will change his mind. There are legal and contractual aspects in every fee. For example, where lie the legal responsibilities for payment when a third party requests a physician to render service to: (1) one's own child, (2) for a relative other than a child, (3) for a stranger, (4) for an employed, or (5) for a child of divorced or separated parents? Simple? Not so, and the authors explain why not.

Under patient-physician relation they include discussion of consent, treatment of minors, and the role of physicians in legal proceedings affecting the mentally ill, each increasingly important.

The subject of medical testimony is of special interest, even though some physicians feel they will never have to give such testimony. They may be unpleasantly surprised sometime to be required to do so. A large percentage of court trials involve medical testimony. The authors' treatment of the subject is an education in the judicial process, especially as it affects a physician. They describe the trial process, the important subjects of privilege and confidentiality, so frequently misunderstood and misused by physicians.

Though physicians are being exposed to a surfeit of malpractice cases in all types of medical publications, this book provides the theoretical background for an understanding of the subject. Most publications deal with the subject on a case by case, state by state basis, the way the law actually is being made. But this does not give an interested physician the background necessary for him to understand the subject as does this book.

The one suggestion I would have for the book is that, in the next edition, it discuss the American system of law to physicians. Undoubtedly they believed that physicians, as educated citizens, understand the law and its administration. They don't, however! This is a minor criticism to make about a book of such excellence.

One of its strongest features is its thorough and complete identification of references. The book is worth its purchase for these alone. If the physician happens to be one of those deeply interested in a subject, he will gain from this book not only a good basic discussion, but all the references he needs for a study in depth.

No matter what a physician's specialty may be, he needs some sort of knowledge in the law as related to his practice. Only the narrow-thinking physician disdains some background in the law. I believe that this book is among the best of the many in its class I have skimmed or read.

SYMPOSIUM ON CARDIOMYOPATHY. American Heart Association. January 15, 1972, Reprinted from Circulation, November 1971, 44:935-968, $1.00.

Review by: LOUIS H. NAHUM

This symposium consists of five papers focusing not on original findings but on teaching. It is limited to a few aspects of cardiomyopathy which are of current interest and importance. The introduction by Dr. Charles K. Friedberg is extensive, covers the subject and almost eliminates the need for reading the other four papers since it covers terminology, diagnosis, prognosis and treatment, but not quite. The other papers are excellent, precise and informative. One by Dr. J. K. Perloff on the cardiomyopathies; current perspectives, is clear, lucid and stimulating.

The other three papers, one by Dr. W. H. Abelman on virus and the heart, illustrates a somewhat neglected, although an extremely practical problem in clinical medicine. The paper by Dr. Timothy J. Regan on alcohol and the heart is a classic in its way and throws important light on one least advertised aspect of alcohol intake in relation to the heart. The final paper is on peripartum cardiomyopathy by Dr. John G. Demaker and Dr. S. H. Rahimtoola.

All in all, the little volume should be available to all physicians and is at the price of a dollar from the American Heart Association.

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LABORATORY SCIENCE ISSUE, Roy N. Barnett, M.D., Guest Editor

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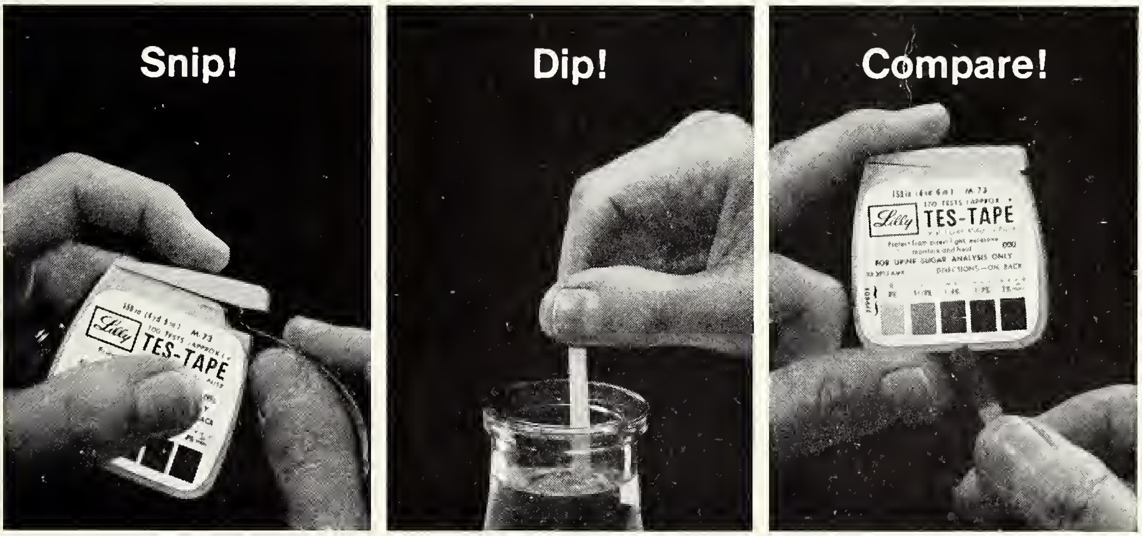

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THE PRESIDENT'S PAGE

Tempting as it may be, the time is past when we, as physicians, can afford the luxury of nostalgia, yearning for, obstinately holding out for, private solo, fee-for-service practice as most of us have known it, and insisting that this is the only form of health care which we can find acceptable. To the extent that we are adamant in our insistence on this as a matter of principle, we will forfeit any influence we may have in shaping the changes in health care delivery which are inevitable. To the extent that the leadership of organized medicine repetitively states these concepts as basic and indispensible to ethical medical practice, it is failing to foster a more flexible attitude among our colleagues. I do not believe, as the media keep telling us, that this country needs and wants radical reform of its medical care system. But I am firmly convinced that to refuse to consider any change in the system of health care is futile, short-sighted and self-defeating. Of course private practice is not dead, is not even moribund, and I hope it will continue to exist. But we must consider the possibility of other modes of health care delivery. In a country as large and diverse as ours, a pluralistic system is desirable.

There are other options than private solo practice, such as foundations or health maintenance organizations. But to establish and successfully operate them it is essential that we have available, information on medical practice not now at our disposal. Foundations seem like a worthwhile experiment and it is for that reason that the Connecticut State Medical Society has encouraged the Hartford County foundation in its endeavors and awaits eagerly the knowledge to be derived from its efforts. To make it possible for such a foundation to succeed, a data base must be obtained so as to make possible peer review and claims validation, and to correct deficiencies and improve patient care.

It is for just this purpose that the House of Delegates, on April 25, 1972, voted to approve a CSMS Ambulatory Care Study. Without the information such a study can supply, it is virtually impossible, from an actuarial standpoint, to establish a successful foundation. This is the path followed in New York where there are at least six foundations, statewide, which are federated and feed their data into a foundation for foundations, the New York Institute for Research and Development in Health Care, Inc. It is this sort of progressive, imaginative action on the part of physicians which offers the best hope for influencing the course of change, and maintaining control over our destiny as physicians. But, equally important, it can achieve improved medical care and correct the prevalent misconception that organized medicine is self-seeking and not at all concerned with the welfare of the public.

It may very well be that foundations will prove to be a desirable method of health care delivery, to be encouraged not only in Hartford but throughout the state. It is for this reason that I plead with all physicans who are approached to participate in the Ambulatory Care Study, to cooperate fully, with the knowledge that they will be contributing to the success of what may prove to be a better medical care system, and most certainly will serve to keep the control of change where it belongs—in the hands of the medical profession.

David A. Grendon, M.D.
President

Multichannel Chemical Analysis In The Medical Laboratory; Medical Usefulness Of The Results

Roy N. Barnett, M.D., Guest Editor

There is no question that devices for multichannel analysis permit medical laboratories to provide enormous amounts of laboratory data reasonably accurately and quite inexpensively. My remarks today are directed to the question; what does all the data mean and how shall it be used in medical practice?[1] I shall use the Technicon SMA 12/60 as the prototype of the multichannel instruments because of its widespread use.

Reliability of Analyses

One of the common assumptions in comparing manual with automated determinations is that automated manipulations are less prone to random error. The generally small coefficient of variation for SMA analyses substantiates this point of view. However there is one channel, the colorimetric GOT, which notoriously suffers from large erratic variation; this produces bizarre results which we would consider mistakes if produced by human analysts; this problem is inherent in the machine.

Abbreviations

CV = coefficient of variation. This is a measure of the dispersion of values about a mean, calculated as

$$\frac{\text{standard deviation} \times 100}{\text{mean value}}$$

SMA; SMA 12; SMA 12/60; used synonymously to refer to a 12 channel instrument produced by Technicon, Tarrytown, N.Y.

Nor is the CV the same in different laboratories all using the SMA 12/60. Table 1 lists results when a series of laboratories in one state performed daily analyses of pooled material from a single source. About 20 analyses in a single calendar month were performed in each installation; the outlying laboratories and values were excluded, so that the tabulation includes only values which fall within chosen limits.

TABLE 1

VARIATION WITHIN METHODS

Test	*Method*	*Mean Value*	*CV (%)*
Sodium	SMA	136.2-140.0	0.7-1.8
Sodium	Manual	137.0-144.6	0.6-3.2
Glucose	SMA	71.7- 90.4	1.5-8.4

Note that the CV for SMA varies from 0.7% to 1.8% for sodium and 1.5% to 8.4% for glucose. I have also included "manual" sodiums to indicate that manual methods may be as good as automated or considerably worse. It is apparent that a CV of 8.4% for glucose in a single laboratory is quite large; for example if the true value of a sample were 110 mg. then the 95% confidence limits for a single analysis are from 92 to 132 mg., or from quite normal to definitely hyperglycemic by SMA chart limits.

Another problem illustrated in this Table is that of systematic rather than random divergence from expected values. For glucose there is an 18.7 mg. spread of mean values between 2 laboratories using the same type of instrument. This means that patients whose values were 92 to 110 mg. in the "low" lab, therefore within the chart normal, would be 111 to 129 mg. in the "high" lab, therefore all above normal.

Nor is this bias only between individual SMAs. Table 2, based on 12 College of American Pathologists surveys in 1970 and 1971,[2] and containing data from hundreds of laboratories, indicates that the SMA 12s as a group yield glucose levels averaging 6% higher than the reference method, the manual O-toluidine.

DR. ROY N. BARNETT, Director of Laboratories, Norwalk Hospital, Norwalk, Conn.; Clinical Professor of Pathology, Yale University School of Medicine, New Haven, Conn.

TABLE 2

RANKING GLUCOSE MEANS

Method	*Average % Difference*
SMA-12	+6.0
Folin-Wu	+4.9
Ferricyanide (Auto Analyzer)	+3.7
Hycel Carbohydrate	+1.9
Hexokinase, Manual	+1.8
O-Toluidine, Automated	+1.7
Hycel PMS	+1.0
O-Toluidine, Manual	—
Somogyi Nelson	−0.4
Glucose Oxidase, Manual	−3.6
Glucose Oxidase, Automated	−5.0

This systematic bias is quite large. Results by this method are higher than those by the Folin-Wu which is generally considered obsolete because it measures considerable non-glucose reducing substances. These high SMA glucose values have led to an epidemic of glucose tolerance tests in many parts of the United States.

We may summarize this section then by saying that this multichannel instrument yields good CVs in some hands and poor in others; that there is a systematic bias between different laboratories using the same instrument; and that for glucose at least the methodology utilized gives results higher than those of any other commonly used method.

Problems of Interpretation of Individual SMA 12/60 Channels

I shall discuss these in the order listed on the SMA 12/60 profile chart[3] and I will make certain presumptions. First I will presume that the physician will inspect the results, and secondly that each abnormal result will lead him to careful thought. As to both presumptions, Williamson's[4] studies suggest that they are excessively sanguine. Furthermore if the physician concludes that the observed abnormality is erroneous, inexplicable or useless, one cannot applaud its acquisition.

A. *GOT*

The erratic behavior of the colorimetric GOT channel has already been mentioned. The complications of false high readings are self-evident; ("do you really only have two Martinis before supper?" "Yes, you have had a heart attack and we will keep you in bed for 6 weeks.") In certain clinical settings the GOT is one of the most useful diagnostic tests. Yet it is quite nonspecific, rising in diseases of heart or skeletal muscle, liver, pancreas, erythrocytes, kidneys, skin and brain, so elevations in very sick patients may be impossible to ascribe to a specific organ system.

B. *LDH*

This is another enzyme elevated in a number of different organ system diseases. Elevations may be marked in certain hemolytic anemias and offer a useful diagnostic aid; however, in vitro hemolysis such as may occur in drawing or processing blood samples also gives high readings. Some recent studies we performed* indicate that in vitro hemolysis just visible as a brownish color of the serum elevates the LDH by about 20%.

C. *Uric acid*

In screening asymptomatic patients uric acid elevations are commonly found and rarely explained. Certainly clinical gout is present in only a few of these patients. So far there is little evidence that treating asymptomatic hyperuricemia does any good, and if allopurinol is used toxic effects may be serious. In hospital patients uric acid elevations are even more common and no more helpful diagnostically. Elevations in uremia are the most common but are not proportional to degree of renal failure, and are less informative than the BUN or creatinine. Starvation may lead to considerable elevations. The utility of this test when not specifically indicated is very low.

D. *Inorganic phosphorus*

Elevations in hospital patients are usually due to renal failure; they are more useful than uric acid in this context.

Very low values occur in starvation and excess administration of fluids (often, alcohol ingestion; less often, IV glucose in water). If this test were omitted from the multichannels very few physicians would request it except for special cases.

E. *Urea nitrogen*

There is little question that unexpected elevation of urea nitrogen is one of the most common findings in chemical screening; in fact Schoen (5) found that 70% of unexpected abnormalities were produced by urea and glucose. Discovery of urea elevations often lead to important diagnoses such as renal failure or gastrointestinal hemorrhage. Low values are almost always the result of excessive fluid administration. Although theoretically urea nitrogen values should be low in acute liver failure I have found this extremely rare and of no clinical utility.

---

* Loc. cit.

F. *Glucose*

High glucose values are also frequent findings in chemical testing, and are often interpreted as suggesting diabetes. If the specimen is taken in the fasting state a high value often signifies diabetes if one makes due allowance for the following factors:

1. *Age*—there is a rise of about 10 mg from youth to old age in men and 15 mg in women.[6]
2. *Recent ingestion* of carbohydrate by accident or design.
3. *Systematic bias*: the high SMA 12/60 values have already been mentioned.

If we acknowledge that the fasting glucose determination is not the ideal test for finding diabetes, missing about one-half to three-quarters of cases, then we must require specimens following a challenge dose of glucose. This can be done by giving pure glucose or high carbohydrate meals. With either challenge the time of day is critical; there are many more "afternoon diabetics" than "morning diabetics". The time post-challenge is also critical; should it be one hour or two hours? After beginning or ending the meal? There is no unanimity of opinion on either of these questions.

Albumin

This channel has caused substantial problems in analysis; methods have been changed because of unreliability of assay. Clinically low albumin is important in assaying the nutritional state of chronically ill patients; it has little or no value in patients clinically well. Frequent repetitions of this test are rarely useful.

Alkaline Phosphatase

In our experience the commonest cause of unexpected elevations are youth and Paget's disease. Children and adolescents may have levels 2 or 3 times those of adults. Paget's disease is not presently a useful diagnosis in that treatment is still experimental. Other disorders such as metastatic malignancy to bone or liver are certainly important to diagnosis although treatment is often unsatisfactory. In hospital patients this is a useful test; for testing well persons it is much less necessary.

Total Protein

High protein levels are found, although rarely, in myeloma and certain inflammatory diseases which elevate globulin. Calculated globulin by difference between total protein and albumin is useful in diagnosis of these inflammatory diseases and in chronic liver disease. The significance of low total protein is about the same as that of low albumin.

Bilirubin

This is a blood constituent which is influenced by diet, being elevated by fasting although rarely to abnormal levels. The values for normal persons are skewed to the left rather than distributed normally; the normal upper limit should be considered somewhat higher than the 1 mg/dl indicated on the SMA chart. Truly elevated values are almost always important clinically except for the constitutional hyperbilirubinemias which are not serious nor treatable disorders.

Cholesterol

Elevated cholesterol values are certainly significant although our knowledge of normals is limited. This is particularly true of those elevations associated with aging; are they normal and harmless, or are they a continuing major factor in the pathogenesis of arteriosclerosis? Values are often falsely depressed for several weeks after a myocardial infarction[7] so the determination in hospital patients is less useful than in generally healthy persons. Low cholesterol values are rarely significant.

Calcium

The recent "epidemic" of so-called parathyroid disease diagnosed primarily as hypercalcemia found by chemical screening leads to certain very serious questions in my opinion.

1. Are all the so-called "adenomas" or "hyperplasias" correct and genuine diagnoses? Some of the illustrations of Black and Haff[8] for example are singularly unconvincing.

2. Why do some of the patients continue to exhibit asymptomatic hypercalcemia after removal of the parathyroid "lesion"? Is it possible that such persons have a normal "calcostat" set higher than usual?

3. Suppose these patients were not discovered and not treated before they developed symptoms? Might they be better off?

Low calcium values are often interesting but rarely very helpful in diagnosis or treatment.

I would like to turn now to the results of chemical screening, using data from Metropolitan Life Insurance personnel as reported in their September 1971 Statistical Bulletin.[6] The cases are well studied and the documentation satisfactory; the results are quite similar to those of Young.[9] The following Tables are slightly modified.*

Summary

TABLE 3

Positives	*Number of Cases*	*Percent*
New positives	24	2.4
Recognized disease entity	11	1.1
Pathophysiological biochemical syndrome	13	1.3
Confirmatory positives	38	3.8
Unclassified positives	190	19.0
Negatives	748	74.8
Total	1,000	100.0

TABLE 4

NEW POSITIVE TABLE

Recognized disease entity	*No. of Cases*
Diabetes mellitus	11
Alcoholic liver disease	3
Pagets disease	2
Hyperparathyroidism	2
Cholelithiasis	1
Drug hepatitis	1
Pathophysiological biochemical syndrome	13
Primary hypercholesterolemia	7
Hyperuricemia, secondary to hypertensive therapy	5
Constitutional hyperbilirubinemia	1

We note that there were considerably more "confirmatory" than "new" positives; their value in screening is minimal.

As to the unclassified positives there were 190 abnormalities not considered significant. This is 8 times as many as all those considered new positives; it also means that for every 1000 patients screened the physicians thought seriously about abnormal results in 190, and finally concluded that they were meaningless!

Of the recognized disease entities it seems that 11 were recognized in the glucose channel; 4 in the calcium; and presumably 5 in the GOT, possibly also in the bilirubin and alkaline phosphatase. Of the biochemical syndromes 7 were abnormalities of cholesterol, 5 of uric acid and 1 of bilirubin. Probably then the 5 other channels contributed nothing. The uric acid abnormalities due to medication, if medically important, would seem appropriately determined as a specific precautionary measure ordered by the family physician; if not medically important they seem academic. One might therefore conclude that all of the abnormalities of any screening significance were contributed by 6 of the 12 channels.

Major and Minor Abnormalities

Rardin[10] used the concept of "significant" versus "non-significant abnormalities," the former being about 1/5 of the total. This is probably a useful approach for screening, in that only values considerably different from the accepted normal range lead to any definitive action. Just where the line is to be drawn is an arbitrary decision and will vary for each of the constituents tested.

In a general way unexpected values beyond the usual 95% range should be checked by observation; values beyond the 99.7% range should lead to repeat testing and contemplative evaluation.

From the viewpoint of the medical usefulness of unexpected abnormal values detected by multichannel screening the 12 tests commonly performed are not of equal usefulness. They may be classified as follows:

TABLE 5

SCREENING APPARENTLY HEALTHY PERSONS

1. Frequently abnormal, information often useful: GOT, glucose, bilirubin, cholesterol, calcium
2. Frequently abnormal, information not very useful; uric acid, alkaline phosphatase
3. Rarely abnormal; LDH, phosphorus, urea nitrogen, albumin, total protein

TABLE 6

SCREENING HOSPITAL PATIENTS

1. Frequently abnormal, information often useful; GOT, LDH, urea nitrogen, glucose, alkaline phosphatase, bilirubin
2. Frequently abnormal, information not very useful; uric acid, phosphorus, cholesterol
3. Rarely abnormal, information often useful, albumin, total protein, calcium

Summary and Conclusions

A brief critique of the reliability and medical usefulness of the 12 tests commonly performed on the Technicon SMA 12/60 is presented. The conclusions as to the medical usefulness of these tests are equally applicable when they are performed by other methods.

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Letters, Notes, And Computers

The Evolution Of A Laboratory Information System

Richard L. Reece, M.D.
and
Russell K. Hobbie, Ph.D.

The Idea

In 1923 two Yale graduates wrote a prospectus about a weekly magazine. The prospectus contained a unique idea—an idea that was to grow into a publishing empire.

They expressed it this way: "People in America are, for the most part, poorly informed.

"This is not the fault of the daily newspapers; they print all the news.

"It is not the fault of the weekly 'reviews'; they adequately develop and comment on the news.

"To say with the facile cynic that it is the fault of the people themselves is to beg the question.

"People are uninformed BECAUSE NO PUBLICATION HAS ADAPTED ITSELF TO THE TIME WHICH BUSY MEN ARE ABLE TO SPEND ON SIMPLY KEEPING INFORMED."

The young men were Briton Hadden and Henry Luce—founders of *Time* magazine.

In concluding their prospectus, they said: "To keep men well-informed"—that, first and last, is the only axe this magazine has to grind. The magazine is one of news, not argument, and verges on the controversial only when it is necessary to point out what the news *means.*"

The Start of System

When I started the *Lufkin Laboratory Letter* in 1968, I too only had only one axe to grind—to keep intelligent busy clinicians as well-informed as possible in a brief, organized, and convenient manner.

Today I would like to describe how our campaign to inform clinicians has fared and what shapes and directions it has taken.

My Thesis

First my thesis, which I paraphrase from Hadden and Luce.

Clincians in America are, for the most part, poorly informed about laboratory results.

This is not the fault of the medical journals; they print all the facts.

It is not the fault of "conferences" of clinical pathological events; they adequately develop and comment on the facts.

To say with the facile cynic that it is the fault of the clinicians themselves is to beg the question.

Clinicians are uninformed BECAUSE NO LABORATORY REPORTING SYSTEM HAS ADAPTED ITSELF TO THE TIME WHICH

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DR. RUSSSELL K. HOBBIE, School of Physics and Astronomy, University of Minnesota, Minneapolis, Minnesota.

BUSY CLINICIANS ARE ABLE TO SPEND ON SIMPLY KEEPING INFORMED.

If I may carry the comparison still farther, laboratories have generally failed to point out what the results mean.

"Abnormal" Results

This is particularly true of the "abnormal" result. Consequently, clinicians often ignore or fail to follow up the abnormal result. If you doubt this, I invite you to read an article in last week's *Archives of Internal Medicine* (Schneiderman, L. J. *et al*, The "Abnormal" Screening Laboratory Results, 129:88-90, 1972). In that article, the authors exhibit a table that contains, among other information, these headings: Total "abnormal" tests, Diagnosis made, and Diagnosis not made. In Table 1, I present a modified version of that information.

TABLE 1

OUTCOME OF CHEMICAL SCREENING BATTERY PERFORMED ON 547 PATIENTS

	Alk. Phos.	*Bilirubin*	*SGOT*	*BUN*
Total "abnormal" tests	53	20	7	51
Diagnosis made	7	3	3	6
Diagnosis not made	46	17	4	45

The facile cynic would argue that this poor outcome is strictly analytical incompetence. In other words, if you performed tests accurately, the problem would not exist. I don't believe it. I say this misunderstanding about "abnormal" tests would be minimal if you informed the clinician with every "abnormal" result how the normal ranges shift with age and sex; specifically what the normal ranges are; why some borderline tests are statistical aberrations not analytical errors; and then gave him a list of logical diagnostic possibilities.

This is not to say that proper analysis is not important. It is. It is the bedrock of the laboratory. But it is only part of the information you should provide.

I suspect lack of such additional information is one of the principal reasons why the word "abnormal" always seems to appear in brackets. Putting it in brackets is a sly way of saying that results ain't what they are supposed to be.

I, for one, think we ought to provide the clinician as much brief, organized, on-the-spot information as we can; we ought to give it to him with every abnormal result; we ought to define exactly what we mean by "abnormal"; and we ought to say what abnormal results *might mean.*

When I use the phrase *might mean,* I depart from the magazine analogy. Without seeing or examining the patient, it's folly for pathologists to say conclusively what results mean. After all, the serum is only a window through which to glimpse man's metabolism. Looking through a window is not the same as appraising a house. Still, it doesn't hurt the view if you cut through the tangle of data in front of the window.

Letters, Notes and Computers

In our laboratory, we have three means of informing the clinician: 1) a monthly newsletter; 2) *Diagnotes*; and 3) *SORT. Diagnotes* are simply gaily-colored slips of paper listing diagnostic possibilities, disease patterns, or interpretative comments (figure 1). *SORT*, or *S*ystem *O*rganizing *R*elevant *T*ests, is a computer program that sorts out the abnormals in a multitest profile, puts them together into disease patterns, and lists the correlated diagnostic possibilities.

I started the newsletter in September 1968; *Diagnotes* in March 1970; and *SORT* in January 1971. I'm citing these dates because table 2 contains some figures showing how our number of procedures has changed over the years.

TABLE 2

NUMBER OF PROCEDURES DONE BEFORE AND AFTER INFORMATION SOURCES WERE BEING INTRODUCED

Year	*Procedures*	*Increase*	*% Increase*
Before			
1961	33,000		
1962	42,000	+ 9,000	+27%
1963	50,000	+ 8,000	+18%
1964	54,000	+ 4,000	+ 8%
1965	60,000	+ 6,000	+11%
1966	66,000	+ 6,000	+10%
1967	69,000	+ 3,000	+ 5%
1968	72,000	+ 3,000	+ 4%
After			
1969	90,000	+18,000	+25%
1970	133,000	+43,000	+47%
1971	194,000	+61,000	+45%

The Response

These information sources alone did not increase volume. Fee reductions, better pickup and delivery of specimens, more internal efficiencies, a man in the field: all contributed. Nonetheless, each time we expanded our information services, volume did perk up briskly and clinicians did accept the information we provided.

Now I should like to comment on the techniques

DIAGNOTE®

type II hyperlipoproteinemia

clinical signs - xanthelasma, tendon and tuberous xanthomas, corneal arcus, accelerated arteriosclerosis.

incidence - common (about 1 in 100).

plasma - clear

cholesterol - usually between 300 and 600 mg%.

triglyceride - usually between 100 and 400 mg%.

lipoprotein ELP - beta-lipoproteins.

genetics - when genetic, a dominant trait. may also be sporadic.

age of detection - adults (over 20).

conditions to be excluded - dietary cholesterol excess, porphyria, myxedema, myeloma, nephrosis, obstructive liver disease.

treatment - diet low in saturated fats
clofibrate
beta-sitosterol
bile-acid-binding resins
nicotinic acid
ileal bypass

comments - type II responsible for sizable fraction of premature mortality and morbidity from coronary artery disease. Arteriosclerosis tends to occur early and may be associated with peculiar arthritis. Uric acid usually normal and glucose intolerance no greater than general population.

first step in treatment is diet low in cholesterol and unsaturated fats. no drug completely satisfactory. therapy must be multiple and individual.

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DIAGNOTE®

low total protein

diagnostic possibilities
- congestive heart failure
- chronic disease
- low protein intake
- malnutrition
- malabsorption
- renal insufficiency
- chronic liver disease
- congenital or acquired hypogammaglobulinemia
- leukemia
- lymphoma
- analbuminemia
- peptic ulcer
- ulcerative colitis
- regional enteritis
- acute cholecytitis

normal range depends on posture and age. Note lower limit consistently lower in hospital patients.

	Boys & Men		Girls & Women	
age	office	hospital	office	hospital
6 months	5.3	5.3	5.4	5.4
1 year	5.9	5.9	5.5	5.5
5 years	6.0	6.0	6.0	6.0
10 years	6.1	6.1	6.1	6.1
16 years	6.2	5.7	6.1	5.5
20 years	6.2	5.7	6.1	5.5
30 years	6.2	5.7	6.1	5.5
40 years	6.2	5.7	6.1	5.5
50 years	6.1	5.5	6.1	5.4
60 years	6.1	5.5	6.1	5.4
70 years	6.0	5.3	6.1	5.3
80 years	6.0	5.3	6.1	5.1
90 years	5.8	5.1	6.1	4.9
100 years	5.6	4.9	6.1	4.7

Figure 1

Two Typical Diagnotes. On the left is a note for Type II hyperlipoproteinemia; on the right a note for low total protein.

I use in the three publications. You may wonder why I call the computer a "publication". It's because I think of it as a media for sending messages. Besides, we alter the program almost daily, and the messages, or memos, are always changing.

Newsletter Techniques

In the newsletter, I try to inform, to educate, and even to amuse. Usually I pick a subject the clinicians are complaining about or something that troubles us. Occasionally I use the newsletter to explain what we're doing with *Diagnotes* or *SORT*.

One problem, for instance, that never fails to bother physicians occurs when they get abnormal results on one specimen yet days later get normal results. They reason that the machine is obviously off, for man, as everybody knows, has a stable metabolism.

I approached this problem by going through a week of venipunctures myself and subjecting myself to various physiological stresses (Tables 3-5).

I closed with this:

"Why this experiment on a pathologist?"

Well, in the first place, he was convenient and easy to control. "The pathologist", as Doctor Holmes remarked, "is useful when kept to heel."

In a second (and more saphenous) vein, we used him to illustrate these points:

1. Quality control statistics are not just numbers; they are numbers that represent people.
2. What people do, what they eat, what they drink, and when they do these things influence chemical results more than machine variation.

TABLE 3

QUALITY CONTROL DATA ON ONE SERUM SAMPLE RUN OVER ONE-WEEK PERIOD

WEEKLY QUALITY CONTROL DATA ON ONE PATHOLOGIST

	Mean	*Standard Deviation*	*Percent Variation*
Calcium	9.9	0.1	1.0%
Phosphorus	3.2	0.1	2.4%
Glucose	113	2	1.8%
BUN	15.8	0.4	2.5%
Uric Acid	7.3	0.2	2.7%
Cholesterol	194	6	3.1%
T. Protein	7.5	0.1	1.3%
Albumin	5.0	0.1	2.0%
T. Bilirubin	0.70	0.04	5.7%
Alk. P'tase	27.4	1.1	4.1%
LDH	112	5.5	4.1%
SGOT	38.8	2.7	6.9%

TABLE 4

CHANGES IN SMA-12/60 RESULTS AFTER VARIOUS PHYSIOLOGICAL EVENTS

	Day 1[1]	Day 2[2]	Day 3[3]	Day 4[4]	Day 5[5]	Day 6[6]	Day 7[7]
Calcium	9.9	9.5	9.8	9.6	9.6	9.6	9.4
Phosphorus	3.2	3.6	3.1	3.2	3.4	2.6	2.8
Glucose	113	94	100	89	147*	106	115
BUN	16	19	13	22	15	15	13
Uric Acid	7.3	8.9	7.6	8.5	9.9	7.5	6.5
Cholesterol	194	171	218	185	197	176	184
T. Protein	7.5	6.9	7.4	7.0	7.5	7.0	6.9
Albumin	5.0	4.4	4.9	4.6	5.0	4.5	4.5
T. Bilirubin	0.7	0.7	1.7	0.6	0.6	0.3	0.7
Alk. P'tase	27	27	31	26	29	25	24
LDH	112	105	115	110	104	103	112
SGOT	39	39	53	34	39	37	35

[1] Fasting; baseline; drawn after 48 hrs. of rest; no alcohol. All tests are normal.

[2] Fasting; drawn 13 hours after 3 ounces of gin and high protein meal; note increased in phosphorus and uric acid.

[3] Fasting; in fact, drawn after 36 hr. fast; note bilirubin and SGOT rise.

[4] Fasting; but drawn 12 hrs. after meal containing 1 pound of roast pork; note BUN and uric acid elevations.

[5] Fasting; 6 hours after drinking 15 ouces of 86 proof scotch; note uric acid elevation and glucose rise.

[6] Non-fasting; 2 hrs. after bacon and eggs; specimen 1 + lipemic; note low phosphorus.

[7] Non-fasting; 2 hours after lunch of roast beef, shrimp, and macaroni; serum 1 + lipemic; note low phosphorus.

* Because of 147 glucose, three hour glucose tolerance performed: fasting 106, ½ hour 181, 1 hour 189, 2 hour 142, 3 hour 70. Negative for diabetes according to criteria of American Diabetes Association (Standardization of the Oral Glucose Tolerance Test, Report of the Committee on Statistics of the American Diabetes Association, Diabetes, 18: 299-307, 1969).

3. Quality control is a two-way street. We can control our side of the street to within ± 1-5.% But results on the patient's side may vary considerably more because of factors beyond our control."

Borderline Abnormals

Another problem that plagues physicians are borderline abnormal results. Most clinicians don't know it, but many borderline results are strictly due to laws of probability. I asked Doctor Russell Hobbie, a physicist at the University of Minnesota who has collaborated with me in developing *SORT,* to write a newsletter piece on how often you would expect borderline *results* if you use 95 percent confidence limits and do twelve tests. He responded with a thoughtful little essay titled "The Probability of Abnormal 12-Channel Results in Normal People". Rather than relay to you what he said, I reproduce his essay:

THE PROBABILITY OF ABNORMAL 12-CHANNEL RESULTS IN NORMAL PEOPLE

"When we began to use the computer to compare patients' results to age, sex, and posture dependent normal ranges, the number of clinically well patients who had one or two inexplicable abnormal results destressed us.

It finally dawned on use that such "abnormals" are inevitable. Why? Because "normal limits" are defined as the Mean ± 2 Standard Deviations. Statistically this means that 95 percent of normal people will fall inside normal limits. It also means that five percent of normal people will fall outside normal limits.

One Test vs. Twelve Tests

The 95 percent approach causes little trouble if you're measuring only one test. Being reasonable people, physicians expect a normal person to have a borderline abnormal test occasionally.

The trouble comes when you start measuring twelve tests at once. Then physicians start to complain about the large number of unexpected borderline abnormal results. Yet probability theory dictates that almost half of the normal people on whom you measure twelve tests will have at least one borderline abnormal test.[1,2]

100 Normal People

Let's take an example. Suppose you're screening 100 normal, i.e., healthy, patients in your office.

You can express the probability that one of these patients has a normal value for a single test (say calcium) as 0.95. This means that 95 of the 100 patients will have a normal serum calcium.

So far, so good.

But now take a second test, for instance, glucose. Assume the glucose result is independent of the calcium result. Again you would expect 0.95 (or 95 of the 100) patients to have normal glucose.

The Rub

Now the rub. What is the probability that one of these patients will have both a normal calcium and a normal glucose? Answer: 0.95 × 0.95 × 100, or 90 patients of the original 100. If you keep applying this law of probability to all twelve tests, you arrive at the astonishing conclusion that only 54 of 100 normal people will have all their tests within normal limits.

And here are the other probabilities:

Probability of all tests normal	54%
Probability of one abnormal test	34%
Probability of two abnormal tests	10%
Probability of three or more abnormal tests	2%

TABLE 5

QUALITY CONTROL DATA ON DAILY SERUM SAMPLES OF PATHOLOGIST AFTER VARIOUS PHYSIOLOGICAL EVENTS.

	Mean	*Standard Deviation*	*Percent Variation*	*Ratio of Physiologic to Technological Variation**
Calcium	9.7	0.15	1.5%	No Change
Phosphorus	3.1	0.4	12.9%	4.0 times
Glucose	108	18	16.7%	9.0 times
BUN	16	3	18.8%	7.5 times
Uric Acid	8.1	1.1	13.7%	5.5 times
Cholesterol	183	16	9.0%	2.7 times
T. Protein	7.1	0.2	2.8%	2.0 times
Albumin	4.80	0.25	5.2%	2.5 times
T. Bilirubin	0.80	0.60	75.0%	6.0 times
Alk. P'tase	27.0	2.5	9.3%	2.3 times
LDH	108	4.5	4.2%	No Change
SGOT	40.0	6.0	15.0%	2.2 times

Advertisement

> *"The history of science, and in particular the history of medicine . . . is . . . the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."*
>
> *—George Sarton, from "The History of Medicine Versus the History of Art"*

Would it be useful in clinical practice to have government predetermine drugs of choice?

Opinion

Results of a survey of physicians:

13.3%
Yes, it would be useful.

86.7%
No, it would not be useful.

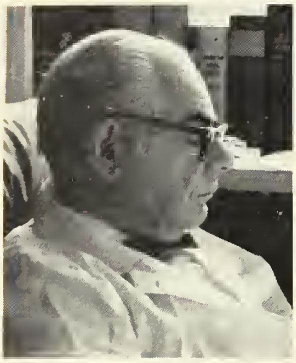
Opinion & Dialogue

Dialogue

Would it be useful in clinical practic to have government predetermine drugs of choice?

Doctor of Medicine

Walter Modell, M.D.,
Professor of Pharmacology,
Cornell University
Medical College,
Editor,
Clinical Pharmacology
& Therapeutics,
Drugs of Choice,
Rational Drug Therapy



The proposition that government should determine one or two "drugs of choice" within a given therapeutic class reflects the belief that a similarity in molecular structure insures a close similarity in pharmacologic effect. But this is by no means the rule. An obvious example would be in the field of diuretics, where a small change in chemical structure accounts for substantial differences in concomitant effects such as potassium excretion.

Any attempt to dictate the "drug of choice" would be complicated by the fact that some populations demonstrate a bimodal distribution in their reaction to drugs. If the data on drug response are mixed for the total population, one drug will appear to be as useful as the other. But if drug response is reported separately for different segments of the population, drug A will be found to be better for one group and drug B for the other.

It may, of course, be possible to determine drugs of choice in particular categories on a broad statistical basis. But there are always certain patients in whom a drug produces odd, unpredictable or idiosyncratic reactions. So, though a drug might statistically be the most useful one in a given situation, individual variations in response might make it the *incorrect* one.

The point I wish to make is that if two, three, four or more drugs in one class are of approximately equal merit, that in itself is justification for their availability. Exceptional cases do arise in which one drug would be useful to a certain segment of the population and another drug would be of no use at all. In the practice of medicine, the physician must be prepared to treat the routine as well as the unusual case.

Another objection to the determination of a drug of choice is that precise statements of *relative* efficacy are very difficult to make—much more difficult than statements of efficacy. For example, in testing drug efficacy, it is easy to determine the difference between a drug that is effective in treating a condition and one that is not at all effective. Thus, it is fairly easy to determine whether a drug is more effective than a placebo. But if you compare one drug that is effective with another drug that is also effective, and the relative differences between them are very slight, statements of relative efficacy may be very difficult to make with assurance.

I do not mean to imply that relative efficacy statements are not useful or can never be made. With some groups of drugs (e.g., analgesics), extensive study and precise methodology have yielded useful information on relative efficacy. But in most situations, such information can be acquired only through studies encompassing three to five years of use in many more patients than are used to compare drugs with a placebo for the introduction of a drug into commerce. It is really only after practitioners use a drug extensively that relative safety and efficacy
in practice can really
determined.

The Bureau of Drugs h
suggested the package i
sert as a possible means
communicating informati
on relative efficacy of dru
to the physician. I find th
objectionable, since I
not believe the physici
should have to rely on th
source for final scienti
truth. There is also a pra
tical objection: Since f
physicians actually di
pense drugs, they seldo
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any event, I would mai
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pending on the governme
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him.

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are swamped by excessi
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the FDA nor any oth
single group has the exp
tise and the wisdom nec
sary to determine the o
"drug of choice" in
areas of medical practice

dvertisement

One of a series

Maker of Medicine

enneth G. Kohlstaedt, M.D.,
Vice President,
Medical Research,
Eli Lilly and Company

In my opinion, it is not
he function of any govern-
ent or private regulatory
gency to designate a "drug
f choice." This determina-
ion should be made by the
hysician after he has re-
eived full information on
he properties of a drug,
nd then it will be based on
is experience with this
rug and his knowledge of
he individual patient who
s seeking treatment.

If an evaluation of com-
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that the established products should not be so easily dismissed.

Variation in patient response to drugs constitutes one of the major obstacles to the determination of "drugs of choice." We are just beginning to open the door on pharmacogenetics, but it is evident that genetic differences cause wide variations in the way drugs are absorbed, metabolized, etc. This fact alone is sufficient to make unrealistic the idea that there is one drug in each class to be used for every human being.

The problem of determining relative drug efficacy is an extremely complicated one. Comparison with other drugs of the same class should not be a prerequisite for marketing a new substance. In some therapeutic areas, it may be difficult to make accurate comparisons. For example, in the treatment of infections it is not possible to conduct crossover studies. Recovery may be influenced by factors which cannot be controlled or measured, i.e., natural host resistance and virulence of infective agents. A drug's acceptability must often be judged on the basis of its own performance, and this may be limited to experience in a relatively small patient population. If the introduction of a new drug must await the adequate establishment of relative efficacy, the duration of clinical trial and extent of studies would be greatly prolonged, particularly for rare or unusual conditions. The availability of a new drug would be delayed. Many patients might suffer needlessly and lives might be lost.

Relative efficacy can best be established by experience in a general patient population through regular channels of clinical practice. The physician considers the patient as a whole, which means the patient often has multiple problems and drugs must be selected with this in mind. Hence, a "drug of choice" in an uncomplicated case may not be the best drug for a patient with associated problems. Publication of well-controlled studies in medical journals may provide comparative evidence; discussions at medical meetings, presentations at postgraduate courses, and the new audio-visual technology may bring evidence to physicians on comparative therapy. In a free medical marketplace, a drug that does not measure up will fall into disuse. For example, broad clinical experience has established vitamin B_{12} as the "drug of choice" for the treatment of primary pernicious anemia. No amount of advertising or promotional effort by the manufacturer could increase the use of liver extract for this anemia. However, a physician may wish to employ parenteral liver preparations for a special purpose.

In the field of surgery, peer review in the hospital has brought significant improvement in the use of new techniques and procedures. Something of this nature would be useful in the area of drug therapy. However, it should be developed by the medical profession itself and would necessitate, for its proper function, an improvement in the dissemination of reliable data on clinical pharmacology of drugs under consideration.

Ideally, information on the relative efficacy of drugs should be gathered and assessed by the physicians who actually administer the specific agents to a specific patient population. To do this, they will need even more information on the drugs they use – information that the pharmaceutical manufacturers must begin to provide if government regulation of *"drugs of choice"* is to be avoided.

Opinion & Dialogue

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Your Problem

What does this mean to you? It means that if you screen normal individuals with 12-channel chemistry graphs, borderline abnormal results are inevitable if the mean ± 2 Standard Deviations, or 95 percent confidence limits are used to define normal. It also means that many of these borderline abnormal results will be clinically insignificant.

Our Solution

Is there some way to retain the traditional 95 percent limits, yet identify the borderline results? We think so. Our SORT computer printout will identify those results falling outside 95 percent limits as ABNORMAL RESULTS. But if all of the results which fall outside 95 percent limits (Mean ± 2 Standard Deviations) are inside 99.7 percent limits (mean ± 3 Standard Deviations), the SORT program will type: ALL TESTS ARE BORDERLINE AND MAY BE PHYSIOLOGICAL AND CLINICALLY INSIGNIFICANT. (see attached SORT printout)

Your Decision

We believe this approach will not only identify those patients with potential early disease but will flag for you those whose abnormal test results may be due to statistical fluctuation. It's up to you, of course, to decide the cause on the basis of your knowledge of the patient."

R. K. Hobbie, Ph.D.

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Brevity and Relevance

I try to keep the newsletter short: one page usually but occasionally I'll go to four if the subject merits it. The main idea is to keep the newsletter like a mini-skirt—long enough to cover the subject matter but short enough to rivet your attention. The newsletter explains the reasons why; *Diagnotes* and *SORT* printouts list the reasons why.

Convenience and Unobtrusiveness

Diagnotes are simply compact lists of diagnostic possibilities, so organized as to list possibilities roughly in order of probability. These little lists, of which we now have about 100, are geared for convenience and unobtrusiveness. They are convenient because the clinician gets his checklist on-the-spot whenever an abnormal result appears. They are unobtrusive because they are not a formal part of the report. The clinician can discard, dispose of, or ignore them if he wishes.

SORT

We regard *SORT* printouts as large *Diagnotes*—expanded, more flexible lists of diagnostic possibilities. We send these computer reports in addition to SMA-12/60 graphs. Why not discard the graphs and substitute the computer printout? First, clinicians like the graphs. Graphs give them a quick visual image of the pattern. Secondly, to hand out computer printouts and take away graphs would violate our wish to be unobtrusive.

The computer has been more difficult than the newsletter or the diagnostic lists for us to handle psychologically. Computers are impersonal and they do represent a threat—no matter what their apologists say. We are trying to use them as humanly as possible. We do this by calling physicians about unexpected patterns; writing notes on the printout; and just generally using it as a means of transmitting information, rather than as and end it itself.

My attitude about computers is this: if they do not free you up for important things, communicating directly with doctors to help them reach a diagnosis, then don't use computers.

I have been fortunate in working with Doctor Hobbie, who understands the human dimension. We have tried to design our computer report in such a way as to keep them informed in as brief and organized a way as possible. (Figure 2)

Design

The printout measures 8 by 11 inches.

In the upper left corner appears the patient's name, age, and sex. Following this appears the statement: "Normal Ranges assume patient is walking and fasting". We print this if the patient was seen in the office because we assume the patient was ambulatory. If the patient is a hospital patient, the computer prints: "Normal Ranges assume patient is in bed and fasting". We distinguish between normal ranges of office and hospital patients because posture influences normal ranges. These differences are most striking for the lower limits of total protein, albumin, cholesterol, and calcium (Tables 8 and 9).

Normal Tests

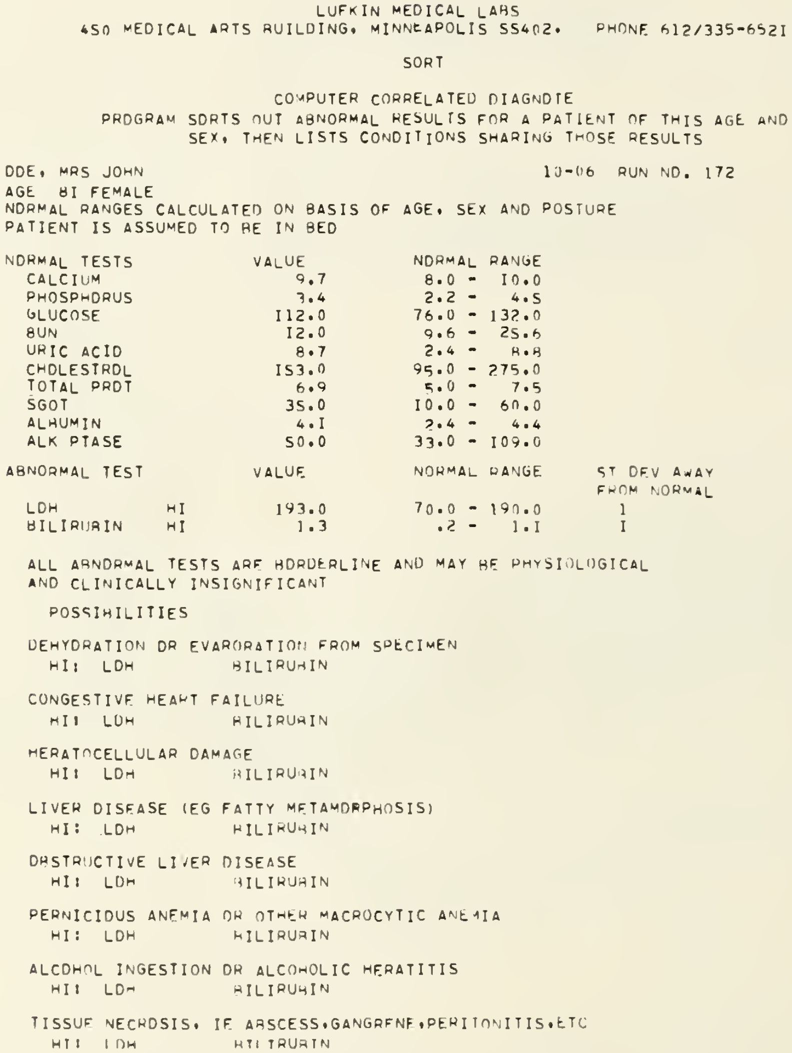
Next you see the column of normal tests with the normal ranges expected for a person of that age and sex. We use shifting normal ranges by age and sex. We determined the ranges on 3349 walking and 863 hospital patients, split equally between the sexes. In arriving at the normal, we relied heavily on visual fits to computer displayed histograms. I realize there currently exists a controversy as to how one should arrive at normal ranges. Doctor Hobbie and I discuss the issue in a paper Doctor Hobbie is presenting in February at the San Diego Medical Foundation. (To appear in the Proceedings of the 1972 San Diego Biomedical Symposium.)

The computer statement has proved extremely

TABLE 7

SUMMARY OF 50 PEOPLE JUDGED NORMAL BY INTERNIST SMA-12/60 DONE ON ALL PATIENTS

	Number of SMA-12/60 Profiles	*Actual Percent*	*Expected Percent*
All tests normal	32	65%	54%
Single borderline abnormal test	9	18%	34%
Two borderline abnormal tests	7	14%	10%
Three borderline abnormal tests	1	2%	2%
Single elevated test, not borderline	1	3%	?
Total borderline tests	18	36%	46%



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                                 SORT

                       COMPUTER CORRELATED DIAGNDIE
           PRDGRAM SDRTS OUT ABNORMAL RESULTS FOR A PATIENT OF THIS AGE AND
                  SEX, THEN LISTS CONDITIONS SHARING THOSE RESULTS

DDE, MRS JOHN                                          10-06  RUN ND. 172
AGE  8I FEMALE
NDRMAL RANGES CALCULATED ON BASIS OF AGE, SEX AND POSTURE
PATIENT IS ASSUMED TO BE IN BED

NDRMAL TESTS              VALUE           NDRMAL RANGE
  CALCIUM                    9.7           8.0 -  I0.0
  PHOSPHDRUS                 3.4           2.2 -   4.5
  GLUCOSE                  I12.0          76.0 - 132.0
  8UN                       I2.0           9.6 -  25.6
  URIC ACID                  8.7           2.4 -   8.8
  CHDLESTRDL               I53.0          95.0 - 275.0
  TOTAL PRDT                 6.9           5.0 -   7.5
  SGOT                      35.0          I0.0 -  60.0
  ALHUMIN                    4.I           2.4 -   4.4
  ALK PTASE                 50.0          33.0 - I09.0

ABNORMAL TEST             VALUE           NORMAL RANGE      ST DEV AWAY
                                                            FROM NORMAL
  LDH           HI         193.0          70.0 - 190.0        1
  BILIRUBIN     HI           1.3            .2 -   1.I        I

  ALL ABNDRMAL TESTS ARE BDRDERLINE AND MAY BE PHYSIOLOGICAL
  AND CLINICALLY INSIGNIFICANT

    POSSIBILITIES

  DEHYDRATION DR EVAPORATION FROM SPECIMEN
    HI:  LDH          BILIRUBIN

  CONGESTIVE HEART FAILURE
    HI:  LDH          BILIRUBIN

  HEPATOCELLULAR DAMAGE
    HI:  LDH          BILIRUBIN

  LIVER DISEASE (EG FATTY METAMDRPHOSIS)
    HI:  LDH          BILIRUBIN

  DBSTRUCTIVE LIVER DISEASE
    HI:  LDH          BILIRUBIN

  PERNICIDUS ANEMIA DR OTHER MACROCYTIC ANEMIA
    HI:  LDH          BILIRUBIN

  ALCDHOL INGESTION DR ALCOHOLIC HEPATITIS
    HI:  LDH          BILIRUBIN

  TISSUE NECRDSIS, IE ABSCESS,GANGRENE,PERITONITIS,ETC
    HI:  LDH          BILIRUBIN
```

Figure 2
SORT printout showing borderline statement

TABLE 8

DIFFERENCES IN LOWER LIMITS OF SMA-12/60 TESTS IN OFFICE VERSUS HOSPITAL PATIENTS

	Calcium			Total Protein			Albumin			Cholesterol		
Age	*Off.*	*Hosp.*	*Diff.*	*Off.*	*Hosp.*	*Diff.*	*Off.*	*Hosp.*	*Diff.*	*Off.*	*Hosp.*	*Diff.*
20	9.0	8.6	–0.4	6.2	5.7	–0.5	3.7	3.5	–0.2	110	105	– 5
30	9.0	8.5	–0.5	6.2	5.7	–0.5	3.7	3.5	–0.2	120	113	– 7
40	8.9	8.4	–0.5	6.2	5.7	–0.5	3.7	3.3	–0.4	130	121	– 9
50	8.8	8.3	–0.5	6.1	5.7	–0.4	3.6	3.1	–0.5	140	121	–19
60	8.7	8.2	–0.5	6.1	5.5	–0.6	3.5	3.1	–0.4	139	113	–26
70	8.6	8.1	–0.5	6.0	5.4	–0.6	3.4	2.8	–0.6	127	104	–23
80	8.5	8.0	–0.5	6.0	5.3	–0.7	3.2	2.7	–0.5	116	96	–20
90	8.3	7.9	–0.4	5.8	5.1	–0.7	3.1	2.5	–0.6	104	88	–16
100	8.2	7.8	–0.4	5.6	4.9	–0.7	3.0	2.4	–0.6	92	80	–12

useful. And for good reasons. It may keep another patient from being labeled with a misdiagnosis; it may get the clinician off the hook; and it may just help clear the air by defining the zone of uncertainty—the gray zone. Ordinary people get the blues; physicians the grays. In any case, in figure 2, I show an example of a borderline printout. In a study we're now doing with a Minneapolis internist, these statistical probabilities have held up well (Table 7). These results are not conclusive, and I'm not pretending they are.

Abnormal Tests

Next comes the abnormal tests. We handle them like the normals except we say if the test is high or low and how many standard deviations it lies from the lower or upper limits. (Figure 2)

Why this standard deviation wrinkle? Because we want to give the clinician some "feel" for how far off the abnormal test is. The Standard Deviation from Normal bit simply gives him a quick impression of the magnitude of the abnormality.

If all the tests are borderline, the computer lists the borderline statement and goes ahead with the differential. If only one test is off, the computer types out the *Diagnote* for that test. With certain very high single abnormal tests, such as an isolated alkaline phosphatase of over 200 units, the computer will type: "An isolated alkaline phosphatase this high generally indicates Paget's Disease, metastatic bone disease, or osteogenic sarcoma." We have other similar statements stored in the program.

Multiple Abnormals

This brings me to the matter of multiple abnormal tests, which seems to be the rule rather than the exception in multitest profiles on sick patients. I am not going into detail here because Doctor Hobbie and I have already done so in the San Diego paper and in a paper that will appear in the American Journal of Clinical Pathology in May 1972.

Diagnostic Possibilities

Briefly, all we try to do is list the top five diagnostic possibilities based on the patient's age, sex, pattern of abnormals, and, in some cases, the magnitude of the abnormalities.

How do we arrive at the first five?

First, the computer matches the pattern of abnormal against its table of disease patterns.

Second, the computer considers only those diseases in which an essential test is present (e.g., an elevated BUN is essential for renal insufficiency, an elevated glucose for diabetes, and so forth).

Third, when certain conditions exist, the computer promotes certain diseases, increases or decreases the match, or deletes a disease.

The important thing about all this is that you can modify the program to fit your criteria for

TABLE 9

DIFFERENCES IN LOWER LIMITS OF SMA-12/60 DURING DIFFERENT TIMES OF DAY AND NIGHT. FIGURES BASED ON 31 VENIPUNCTURES IN HEALTHY 25 YEAR OLD MALE MEDICAL STUDENT OVER FIVE DAY PERIOD

Time	*Calcium*	*T. Protein*	*Albumin*	*Cholesterol*	*PBI*
ERECT					
11 AM	9.1	6.9	3.9	169	4.8
3 PM	8.8	6.7	4.0	166	4.8
7 PM	8.9	7.1	4.1	177	5.0
11 PM	8.6	6.8	4.0	168	5.0
SUPINE					
3 AM	8.2	6.2	3.8	155	4.1
7 AM	8.3	6.3	3.7	150	4.1
Differences between average values of erect minus supine position	—0.6	—0.6	—0.52	—18	—0.8

* Lower limits calculated as mean values minus 2 Standard Deviations for five results at each of indicated times.

arriving at a diagnosis. Just about anything you can articulate about an interpretation can be programmed.

In short, you can automate interpretation just as you can automate tests. So far we find the proper diagnosis appears about 80 percent of the time in the first five possibilities (Hobbie, R. K., and Reece, R. L.: The Use of a Computer to Suggest Diagnostic Possibilities from a Battery of Blood Chemistry Values, to appear in the Proceeding of the 1972 San Diago Biomedical Symposium, February 2-4, 1972).

Conclusion

In closing, I would like to remind you the National Commission on Chronic Illness has suggested five criteria for judging screening programs—reliability, validity, yield, cost, and acceptance. Today I have talked about one way of achieving acceptance.

Acknowledgment: I wish to thank my partners, Doctor Wayne Chadbourn and Doctor John Popowich, for creating an atmosphere that made this work possible and Doctor Richard Frey for his continuing clinical study of multitest results.

Screening Tests And The Detection Of Disease

Roger K. Gilbert, M.B., B. Chir.

When laboratory tests are used for screening purposes, there are a number of fundamental changes in the relationships of tests to the identification of disease. In day-to-day medical practice the physician defines a provisional diagnosis and then selects a laboratory test that will help to confirm or exclude this diagnosis. When a test is used in a screening program there is no provisional diagnosis and the test is performed on a population which is regarded as being at risk for a certain disease. The test result is then used to define whether or not the disease is present.

The transposition that places the test before the diagnosis is readily made. However, this simple reversal results in some major changes in the ground rules that govern the relationship of tests and disease.[1,2] Many physicians are unaware of these conceptual changes and problems arise that could have been anticipated.

Some of the problems and some approaches that may minimize the difficulties will be briefly discussed in this presentation.

The Importance of the Normal Range

There are problems in the selection and definition of normal ranges.[3] Many articles have described these difficulties and suggested a variety of approaches that can be used to establish appropriate limits.[4,5] A further aspect of the normal range is not as widely appreciated. This concerns the relative importance of the normal range in a screening program as opposed to its importance in day-to-day medical care.

The normal range is of minimal importance for many of the day-to-day decisions in the care of the acutely ill. In a screening program it becomes central and much of the success and cost of the program depends upon the exact definition of the limits of normal. There are a number of reasons for this change.

Many of the tests performed on a sick patient in a hospital are carried out to follow levels from one day to the next. Thus, a sodium level may fall or a hemoglobin level may rise. Similarly, a pattern of consecutive enzyme values can be used to support or exclude a diagnosis of myocardial infarction. In each of these instances, the change from one day to the next is the important feature and a series of results are available. The interpretation is not based on a single result and the relationship of this result to a limit derived from population statistics. In addition, the physician who requests a test has a number of options available when he receives the result. He can accept the value and take appropriate action, he can defer action while he follows the patient's clinical course, he can request

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that the test be repeated, or, finally, he has an option to completely ignore the result. His knowledge of the normal range is only one of the many pieces of information that he uses in reaching his decision. He must also consider the impact of the abnormal result on the patient, the likelihood that it is not an artifact, the degree of abnormality of the test and his prior knowledge of the patient's illness.

In contrast, in a screening program there may be no options and it is mandatory to classify each result as either normal or potentially abnormal and take the appropriate action. The only information available for this separation is the test result itself and a set of limits that are defined as the normal range.

These factors combine to make the definition of the normal limits the central underpinning of a screening program. Clinical medicine has survived for many years on a list of normal values that was frequently derived from results obtained in twenty healthy people who chanced by the laboratory at the time the test was being developed. This was less than ideal but for a screening program such a loosely defined range would be a disaster. Screening by definition, is an attempt to detect asymptomatic patients in the early stages of their disease. When this is translated in terms of test results this implies identification while they are still close to the dividing line, the limit of the normal range.[6]

False Positive Results

A false positive result causes a healthy person to be classified as diseased and a successful screening program should produce minimal numbers of false positive results. Unfortunately, there are a number of reasons why both the impact and frequency of false positives may be high in a screening program.

Many of the tests that are used in day-to-day medical care may be abnormal in a number of different conditions yet the tests can be widely and successfully used. A typical example that has already been cited is the use of enzyme levels to confirm or exclude a diagnosis of a myocardial infarction. A similar example would be the use of an alkaline phosphatase level to diagnose hepatic metastases in a patient with a known primary carcinoma. There are many causes of elevation of each of these enzymes yet they can be sensitive indicators of disease when they are related to a clinical premise and are used in conjunction with other pieces of information.

When either test is used in a screening program the situation is very different. In the absence of a clinical premise each of the possible causes of elevation has to be considered and evaluated. When the physician starts to seek these out he may become involved in an undertaking as extensive as the full work-up of a patient with fever of undetermined origin. At the end of this he may still draw a blank.

In addition to the medical sources of false positive test results there are statistical reasons why the number of false positives may be high in a screening program.[7,8] These stem from the methods used to define the normal range. For most laboratory tests the normal range is based on limits that encompass 95% of the population within the normal group. This implies that 5% of the healthy population will yield abnormal results and that for every one hundred people screened there will be five false positive results. If, in addition, the disease that is being sought has a low incidence, say one case per one hundred people, then for every one hundred entering the program there will be five false positives and only one true positive.

This relationship can be damaging in day-to-day medical care and it may prove overwhelming to a screening program.

In day-to-day care a test will function effectively as long as the physician uses some selectivity in choosing which patient he wishes to test. As he lessens his selectivity and applies the test more indiscriminately there will be an inevitable rise in the percentage of false positive results.

Some numerical examples are shown in Table I. The values in the Table are applicable to a wide variety of common laboratory tests, in fact, to any test in which the normal range is calculated to include 95% of healthy people. A typical example would be the use of a thyroid function test such as the T4 for detecting thyroid disease.

The first line of Table I shows that if one in

TABLE 1

RELATIONSHIP OF DISEASE PREVALENCE TO THE NUMBER OF FALSE POSITIVE RESULTS

Prevalence	*Non-Specificity*	*% False Positive*
33 %	5 %	9%
5 %	5 %	50%
1 %	5 %	83%
.01%	.01%	50%

Prevalence = % of population tested who have the disease.

Non-Specificity = % of positive test results in healthy people.

% False Positives = % of all positive results which are false—i.e., occur in healthy people.

(It is assumed that all the patients with disease will show a positive result).

three of the patients tested actually has the disease, then 9% of the positives found will be false positives. However, if the selectivity is dropped to one diseased person in twenty then 50% of the positive test results will be false positives.

The third line shows a situation that could arise in a screening program, either carried out on a healthy population or when a thyroid function test is routinely applied to a group such as female patients with sterility problems. When the prevalence falls to 1%, the number of false positives rises so that four out of every five positives are actually false positives. Clearly a proportion as high as this is overwhelming.

As these relationships progress into diseases of lower prevalence, there will be large numbers of false positives even when the tests that are used are highly specific. A practical example is seen in phenylketonuria testing. A recent article suggested that there are fifteen false positive elevations of phenylalanine levels in neonates for each diagnosed case of phenylketonuria.[9]

The fundamental relationship that is involved is shown in the last line of the Table. When the prevalence is one in ten thousand and the non-specificity is one in ten thousand then 50% of the positives will be false positives, or put in another way, for each ten thousand persons tested there will be one true positive and one false positive.

This ratio would constitute a practical basis for a screening program. By simple proportion as long as the prevalence and non-specificity are equal there will be 50% false positives.

A further comparable problem stems from the method of defining normal range. This concerns the effect of performing multiple tests one each individual patient. Just as testing large numbers of healthy persons will result in an increase in false positives, so doing large numbers of tests on a single patient will result in false positives. There is a direct relationship between the number of tests that are performed on a patient and the chance that one of these, for statistical reasons, will be a false positive.[10]

Thus, for both medical and statistical reasons the number of false positives may be high in a screening program and a large part of the effort of the program may be dissipated in evaluating these patients before it is finally shown, by exclusion of all possible causes, that they are healthy. The potential magnitude of the combined effects of these problems is shown by a recent account of the results of screening five hundred and forty-seven patients. There were fifty-three abnormal results for alkaline phosphatase and this yielded a diagnosis in only seven cases.[11]

Strategies for Success

A screening program becomes more effective as the tests that are used for screening become more specific. Ideally, a screening test should be completely specific. All patients with the disease should have an abnormal test and no healthy patients should yield abnormalities. This relationship is seen in some areas and could be approached in other areas by some changes in strategy.

Complete specificity occurs principally in the area of congenital disease. Transposition of a glutamyl residue by a valyl residue in the appropriate position of a globin molecule is specific for Hemoglobin S.[12] Unfortunately, there are far too few common diseases that can be defined in terms that are as specific as this and there is a large void in the area of specific tests for the common diseases such as arteriosclerosis and cancer.

Among the routine tests, the nearest approach to this level of specificity is seen for the various tests in which the substance that is measured is inherently harmful and the level is proportional to the severity.

The most common example of this relationship is the level of hemoglobin and this has provided a practical basis for large numbers of screening hemoglobin levels. Although one may argue whether 10 gm/dl hemoglobin level is adequate for surgery, there is no argument that this level is an absolute indication of an abnormal state. There are other examples among the routine tests. Two comparable patterns are seen with calcium and cholesterol but in neither is the relationship as clear as it is with hemoglobin.

When there are no routine tests that are sufficiently specific then there is an alternative approach that has not been widely applied. This involves a progressive series of procedures within the laboratory each test acting as a screening procedure for the next more complex step. Theoretically, a progression of this type could be highly specific. It would also circumvent some of the cost problems of utilizing complex techniques because the earlier tests would screen out many of the samples and the costs of the complex tests would be amortized over the whole program. This type of program could effectively remove the problem of false positives from the physician and his patient to the laboratory and would allow a systematized approach.

This progressive system was used, apparently successfully for galactosemia screening.[13] It would appear to offer a possible route for some of the common diseases.

Conclusions

The problems that have been described stem from two main areas. They are effects that result from the statistical overlap between the normal and abnormal population groups and problems that arise from the various medical and physiologic causes of false positive results. They are seen when tests that are useful in day-to-day care are uncritically applied to screening programs. This usually occurs because these tests are readily available. It can also occur because these various tests constitute a readily saleable technology for which there is an eager market.

There is a real risk in this approach that physicians will learn to disregard laboratory tests[11] and that good laboratory tests will earn a bad name.[14] There is also a risk that screening program will fall into disrepute.[15]

Alternative strategies are available but they require substantial development. In the interim it is essential that there is a widespread recognition of the simple fact that screening is a different science from the care of the sick. If we try and screen using our present techniques then we are unlikely to be successful. If problems occur when screening is carried out with twelve tests then it is no solution to move on to eighteen merely because equipment is available that can perform this number of tests. What is needed is thought, planning and defined goals, and then development of a technology to match these objectives.

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Set the example: have periodic health examinations!

Connecticut Medicine

Editorials

Multichannel Chemical Analysis In The Medical Laboratory

The first three articles in this issue are presentations made at a panel discussion held at the Park Plaza Hotel in New Haven on January 19, 1972 by the Connecticut Society of Pathologists. The fourth panelist, Robert E. Westlake, M.D., a prominent internist from Syracuse, New York, did not submit a manuscript.

One outstanding problem in modern medical practice is the increasing division between specialist groups, each of us speaking primarily to his own group, writing for his own group, reading chiefly his own specialty journals. This panel discussion, attended by a few internists and numerous biochemists, was an effort to cross these groups lines.

A remarkable development, evidenced at this meeting and one I have noted often before, is that each specialist develops an almost childlike faith in the skills of other specialists, but remains severely critical of his own field where he knows the pitfalls so well. Thus the Clinical Pathologists constantly warn of the problems in excessive reliance on laboratory data, but believe that clinical examination affords reliable information. Contrarily the clinician, particularly the Internist, tends to develop a great reliance on the "hard data", the so-called "data base" derived from laboratory tests, and deprecates the information he obtains from the patient by interview and physicial examination.

Alvan Feinstein in his usual perceptive fashion pinpoints this dilemma as follows.[4]

"Rather than confronting and solving the problems of clinical data clinicians have substituted the plethora of metric data available from paraclinical technology. —. To achieve the phantasmagoria of metric data in modern medicine, clinicians have shifted their medium of observation from the patient in bed to the substance in the lab."

The multichannel instruments certainly make the acquisition of a huge data base practical; there are newer instruments available and under study which may well double or triple the present test capacity. To use this data intelligently there must be a much more astute use of the technique. A great many analyses performed on samples when the source, preservation and test methods are poorly controlled, will yield a very large data base of little or no value, or even yield spurious evidence for disease or non-disease.

Specific problems relating to analyses, normal values, patient physiology and population selection are examined in some depth in the following presentations. One of the most obvious conclusions is the need for controlled conditions for sample collection; for example the ideal sample for establishing hypertriglyceridemia is not the same as that for diagnosing diabetes. Another conclusion is the need to develop different test batteries for specific population groups and disease problems. Ideally the choice of tests should be entirely a medical decision and not governed by instrument capability. It is certainly illogical to employ the same tests for everyone; furthermore some of the tests commonly done seem to be almost irrelevant to human disease and its diagnosis.

Dr. Reece, in his search for a valid comparison between physiologic and technologic variation of test results has indulged in self-experimentation of a heroic calibre (see Table 4), and all of us owe him not only gratitude but a measure of admiration for these efforts!

The literature in this field has become enormous; a few selected references which are recent and which amplify the material in this issue are listed below.[1-3]

Roy N. Barnett, M.D., *Guest Editor*

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Child Abuse

The current series on the prevention of child abuse by Drs. Trouern-Trend and Martha Leonard is a stimulus to point out two things. One is that the data shows that the grossly abused child represents only the top of an iceberg of a vast reservoir of unwanted children in our society. Secondly, the prevention of the sad disgraceful cohort of unwanted children can be simply stated: parents who do not want children or who are ill prepared to function as parents should not have children. Implementing this proposition is not so simple.

Although our society likes to think of itself as being a child-centered society this is simply not borne out by the evidence. Compared with some European countries which we would not even consider democratic or particularly humane we are clearly second in most of the measurements that can be applied such as neonatal damage or services for the very young in day care centers and the expenditure for such services not to mention that for schools. In the past year alone over half of the school bond issues nationwide were voted down by our adult voters and the President vetoed a bill to provide the funds for day care centers as "too expensive." A "child-centered society" does not behave in this fashion.

Our society ascertains that people who want to drive a car know how to do so, and it makes certain that people who want to get married do not have a venereal disease, but the most important job any of us can undertake, that of being a parent, is assumed to be known to everybody who undergoes or helps produce, a pregnancy. Worse yet, our society including a large sector of our own profession makes it very difficult (specifically in forty-four states which maintain laws forbidding abortion except to save the life of somebody) to behave rationally and seek to prevent the birth of an unwanted child by aborting it before it is viable.

Psychiatrists, professionals and social and penal agencies know of no greater misery than the fate of an unwanted child which is a malignancy on intra- and interpersonal levels every bit as untreatable as most cellular malignancies. Some 300,000 children await adoption in foster homes, mostly foster homes which make their adoption less likely and desirable because they are inadequate, and this despite the tremendous reluctance in every state for the State to assume custody for maltreated children even after gross evidence of malparenting has been presented by us or some social agency.

Unwanted children could be prevented by adequate dissemination of birth control information, and that means dissemination of such information before puberty and a vast educational effort to emphasize and teach parenthood and family responsibilities. However women will procreate beyond their absolute wishes to produce children, and quite often beyond their resources for effective parenthood, if they see no alternative opportunities for productive and gratifying pursuits in their lives. Thus, the adequate and equal preparation of girls for life work and careers is every bit as necessary in order to achieve the prevention of unwantedness as is the technical know-how of birth prevention.

Another myth we indulge in is that we are future oriented, which we are in our instrumental pursuits. But it is time that we became future oriented with regard to human beings and ascertain that we create human beings that are wanted and who will then want children commensurate with their resources, and who will assume parenthood well prepared with respect to the responsibilities involved and as part of a life plan which goes beyond full-time motherhood and housewifery.

Stephen Fleck, M.D.

We Are Not Living Longer Anymore

The life expectancy of man in the U.S.A. has been on a plateau for the last 20 years. It is around 70. During this time we have witnessed the appearance of more new journals, publications and knowledge, training programs, research laboratories and research activities then in any other generation in the history of man. The crash programs, funds, and effort in research of the past generations have barely added one year to the life expectancy of man, the one who is supporting the research. Indeed, in spite of the "advancements" in medicine, "criterion" medicine and the new procedures, apparatus, and many provisions for medical care the life expectancy of the American may actually be declining. Why should this be so? Why so little realized?

It has been estimated that the discovery of a cure for cancer will add only about 1.5 years to man's life expectancy and a cure for all cardiovascular and renal disease, the champion killer, will add only 7 to 5 years (2 to 3). However, if the diseases of society such as war, accidents, alcoholism, drug abuse, pollution, industrial hazards should grow as medicine conquers disease, it could be conceived that the life expectancy might even decline. In addition, if people fail to accept personal responsibility for their individual health such as obesity, smoking, then an added counterweight to the contribution of medicine to longevity could make the average length of life decline further.

One hundred million people drink alcoholic beverages and of these there are 9 to 10 million alcoholics. The loss of life, the invalidism and premature death is surely a counterweight to medical science contribution to longevity. There are 56 million smokers in this country. Their morbidity is high and mortality premature by anywhere from 8 to 16 years. There are almost 1 million drug addicts whose longevity is very short and morbidity very high. The number of obese in our population is not accurately estimated but 30 percent develop hypertension, 30 percent develop diabetes. Their longevity is definitely reduced.

There are approximately 44 million accidents yearly of whom 11 million need medical help. There are 55 thousand deaths on the road yearly and 2 million accidents, many serious. The inroads of pollution, air and water, upon human health has not been clearly delineated. With such increasing counterweights to the benefits from medical care it is not surprising that mortality figures should not decline. Furthermore, with so many features of our society that is dragging the average life span down, it is hardly correct to blame medicine with all its accomplishments for not increasing the life span.

A great problem, of course, limiting longevity is the aging process. Once society takes serious steps to cure itself of its deficiences, it will be the fundamental process of aging which needs to be researched if man is to live much longer in good, vigorous, youthful health.—L.H.N.

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Research And Ethics

The magnitude of the loss of life, the suffering and destruction associated with the dropping of the atomic bombs upon cities in 1945 caused a great deal of soul searching by those directly or indirectly involved in the research which made possible the construction of the bombs. The major question facing the nuclear physicists was whether they were morally responsible for the havoc which ultimately resulted from their work. Is a scientist responsible for the use which others make of his discoveries? If a scientist believed that the government or some other body was using scientific knowledge for dangerous or immoral purposes or if he believed that research in certain areas would produce information that might be misused did he have a responsibility to inform the rest of the citizenry of the situation?

A number of authors have expressed their opinion on the subject. The statement of principles of the Society of Social Responsibility in Science is fairly representative of prevalent attitudes and assigns to the scientist the following obligations.[1,2] First of all he must try to foresee as far as possible the result of his professional work. Secondly, he must assume personal moral responsibility for the consequences of this work and not delegate this responsibility to his employer, in the case of the physical scientist to the government. Thirdly, he must put his own efforts only into that work which he feels will be of lasting benefit to mankind. Finally, he must share his scientific knowledge and such ethical judgments as are based upon it, with government and layman alike, in order that they may intelligently use the tools which science provides.

During the same year that the physical scientists were wrestling with their consciences there was a parallel development of ethical concern in medical research. The medical profession and particularly those engaged in research involving patient care were profoundly shocked by exposure of the so-called "medical experiments" which doctors carried out in Hitlerite Germany. Unlike the nuclear physicists, the medical scientists were not concerned about the use to be made of their discoveries since they thought they were gaining medical insights into disease and learning how to prolong human life. Their concern was with the methods to be used in their experiments and the ethical validity of performing experiments on human subjects.

This matter as dealth with by several bodies laid particular emphasis on the concept of "informed consent" by the patient subject. Statements such as those of the World Health Association[3] appeared to offer adequate guidance to medical researchers. Recently, however, the development of knowledge in the field of medical genetics, has presented the medical profession with the same problems which the physical scientists faced 2 decades ago. The ability to exert large scale genetic control of the population may not be far in the future. Researchers whose work will provide this power should be asking whether they will be morally responsible for any misuse of this power. Like the physical scientists they must now give some thought to the ethical problems associated with the goals of their research as well as the procedures used in this research.

How does one aproach such problems to obtain valid and self-consistent answers? In a recent book, Ethics for Scientific Research[4] Reagen reviews the principles of various ethical systems and demonstrates the application of such concepts to specific cases in which ethical problems arise. This presentation makes clear that ethical concepts for scientific researchers are not different from those of nonscientists. They are based on the same belief in a set of moral values and on a set of obligations or rules for behavior designed to achieve the "good." Problems arise in the application of these values and rules to specific research projects. Is knowledge itself one of the highest values? Is the geneticist doing "good" if he provides knowledge which others can use for "evil."?

Clearly the medical scientist must decide on the priorities of his values and must adopt a set of principles comparable to those of the physical scientists that will govern the direction of medical research. Such a set of guidelines can act as a conscience about the fate of society and of man as an individual.

Those engaged in medical research should be aware of three major areas in which they are most likely to err. The first is the failure to recognize what constitutes medical research. For example, many physicians are performing experiments whenever they use therapeutic or diagnostic procedures. Very careful records of the results would offer a great opportunity to contribute to knowledge. The second area of error is the frequent failure to obtain meaningful consent from the subject. The investigator will be completely honest with himself in balancing the value of his work against the demands he is making on the patient. Being convinced of the validity and importance of his work he should be able to explain the goals, benefits and dangers of the research with sufficient clarity that the patient has a rational basis for consent. Lastly, there is the failure of medical scientists to explain to laymen the nature of his work and the potential use and misuse of his findings.

It must be born in mind that the consequences of some research are entirely unpredictable and cannot even be forseen. Could Sir Alexander Fleming have predicted when he observed lysis of a colony of bacteria alongside of a mold contaminated (penicillium notatum), that it would lead to conquest of infectious disease, prolongation of life, a large aged population, social security, increasing need for hospitals and medical care? Or could Lisa Meitner who observed atomic fission and enormous amounts of energy so liberated, have predicted the atomic bomb, the struggle between nations, the terror of unleashing an atomic catastrophy as well as nuclear energy—a human "good?"

The fact is that basic research can lead to totally unpredictable consequences and that only moral man can deal with them. Knowledge is good but only a "good" man should be in posession of it.—L.H.N.

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The Clinical Use Of Calcitonin

Calcitonin, discovered in 1961 by Canadian scientists, is a hormone that has a profound role in the preservation of calcium balance in the body. At first it was thought to be secreted in the epithelial cells of the thyroid and was called thyrocalcitonin. In 1967 it was found also by Canadian scientists to be derived from an embryologically distinct tissue ultimo-branchical bodies fused during the development of the thyroid. Its exact role in the body and its mode of action are still largely unknown but interest is now focussing on the possible applications of the hormone in clinical medicine.

There are in fact a number of calcitonins each with a 32 amino acid and single-chain polypeptide structure but varying in detail according to species. An injection of the calcitonins cause a rapid fall in the plasma calcium level. The interesting clinical effect is to inhibit resorption of bone and moreover to exercise this effect more markedly where resorption is faster than normal. Three such clinical situations occur, Paget's disease of bone, osteoporosis and other demineralizing bone disorders.[1]

Paget's disease is a common disorder of bone which occurs more frequently in older people, is often asymptomatic at which time it is detected only on casual radiography. There are, however, patients in whom there is considerable suffering because of bone deformity, bone pain, particularly headache, fractures, loss of hearing or the complications of bone sarcoma.

It is a mysterious disease. There is an excessive rate of bone resorption and formation and there is also an increase in the number of bone cells. The increased activity in bone is associated with a rise in the serum levels of alkaline phosphatase and in the urinary excretion of hydroxyproline, which is a product of bone breakdown. Injections of calcitonin not only inhibits bone resorption but also lowers urinary hydroxyproline and serum alkaline phosphatase.[1] A combined study from London and Paris[2] now reports that in 5 cases of Paget's disease treated with human synthetic calcitonin, a return to normal of the biochemical abnormalities was achieved.

Woodhouse gave .05 mg. of calcitonin in 1 ml. saline by intramuscular injections three times a day for 11-14 days. First, however, they made control observations for 9 days before undertaking treatment. After the course of treatment, the patients were discharged from the hospital on 0.5 mg. twice daily. On the first day of treatment the serum calcium and phosphatase levels, fell toward normal. The urinary hydroxyproline excretion fell to normal within days.

They also took bone biopsy specimens and observed the changing histological picture during treatment. Paget's bone shows a peculiar fibrous or woven structure with large numbers of osteoclasts. After treatment the new bone showed a normal lamellar structure with a striking decrease in the number of osteoclasts and a drop to normal in the numbers of nuclei. The amount of bone undergoing resorption also decreased as did the rate of calcium uptake by bone. In as much as the polypeptide had the structure of human calcitonin, no antibodies were formed during and after treatment.

A most gratifying feature of the trial is that all five patients experienced complete relief of bone pain while the side effects of the calcitonin were minimal. It thus seems likely that in addition to relieving pain, calcitonin may prevent deformities of Paget's disease by laying down a more normal bone pattern.

An entirely different approach to the treatment of Paget's disease of bone has been opened by Smith, Russell and Bishop[3] who report on the value of diphosphonates which have the peculiar property of acting as crystal poisons, i.e. they may inhibit crystallization, crystal growth or even crystal dissolution. Thus they may interfere with bone turnover and might be expected to slow down the process in Paget's disease in which the turnover may be 50 times the normal.

Smith gave 20 mg. of diphosphonates disodium etidronate per kg. body weight by mouth daily to four patients. He found that the drug did indeed slow down bone turnover and led to reduction in urinary hydroxyproline levels as well as reduced alkaline phosphatase levels. There was also some relief of symptoms.

Here then are two promising approaches to a fairly common disease. We still await extended experience in the use of calcitonin in patients with osteoporosis. Very promising results have been reported in a few patients.[4] Even if it did no more than slow down and arrest the process this would already be an advance in the commonest disease of mankind. Its reversal would be a boon of unparalleled importance.—L.H.N.

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Correction Of Hyperlipoproteinemia

It is now possible to correct high lipid and lipoprotein levels substantially in almost all patients with any one of the familial hyperlipoporteinemias. No single treatment is applicable to all of them, since each has its own distinct requirements. In familial type I the metabolic difficulty is an inability to hydrolyze triglyceride derived from the fats in the diet. Normally a heparinoid enzyme accomplishes this. Persons who do not have this enzyme absorb the unhydrolyzed fat in the form of chylomicron particles which accumulate in the plasma and are deposited in arteries. Restriction of dietary fat quickly reverses the chylomicronemias. To make the diet palatable and to avoid over consumption of carbohydrates for this may undesirably boost pre-beta lipoprotein levels. 25 g. of dietary fat is allowed daily. Medium chain tryiglycerides (MCT) is a useful supplement since unlike conventional dietary triglycerides it does not rely on chylomicron formation for transport. Instead its fatty acid constituents travel directly to the liver in the portal circulation.

The raised beta lipoprotein cholesterol levels in the familial type II hyperlipoproteinemia can be reduced about 25 percent on an average by a diet low in cholesterol (less than 300 mg daily). The main features of the diet are the elimination of egg yolk in any form, restriction of dairy products and avoidance of fatty acid organ meats and shellfish. Palatable low cholesterol cooking oils and other substitutes are commercially available. Frequently completely normal lipid blood levels are not achieved on such a diet. So something else is needed. Several drugs such as estrogen, d-thyroxin clofibrate have in different instances proved reliable in achieving and maintaining normal lipid levels in hyper beta lipoproteinemia. Many patients do not respond even with these drugs then resort to the resin cholestyramine often yields encouraging results.

When added to a low cholesterol diet it usually produces further and often substantial falls in cholesterol levels and they are often maintained sometimes to the point of a normal beta lipoprotein level. The action of this ion exchange resin rests on its ability to exchange chloride ion for bile acids in the intestines leading to increased excretion of bile acids. The acids are derived from cholesterol and despite increased production of cholesterol in the liver, the net result is a fall in total acid beta lipoprotein cholesterol in normal persons and in patients with hyperlipoproteinemia.

However, the use of cholestyramine resin should probably be restricted until further research has been completed. At present its administration to patients with severe hyperbeta lipoproteinemia is justified especially when they are young and free from symptoms and when there is a family history of premature vascular disease. One needs to bear in mind some adverse effects of the resin alone. It may bind certain drugs and interfere with their absorption and particular care is needed if it is given with oral anticoagulant drugs. Other drugs should be given at least 30 minutes before a dose of resin. Finally, is the problem of constipation which the resin induces and which can be most destressing.

The treatment of familial type III hyper beta lipoproteinemia is especially gratifying since it consistently results in total correction of hyperlipemia although the abnormal beta lipoprotein form persists in low concentration. The treatment is of three parts. Low cholesteral diet, reduction to ideal weight, and its maintenance on a balanced diet in which fat and carbohydrate each provide 40 percent of total calories together with clofibrate 1 gram twice daily.

The person with increased pre-beta lipoprotein levels due to familial type IV is usually fat and reduction to ideal weight and its maintenance by a balanced diet often sufficies to reduce lipid levels substantially. If such a regimen is not enough then clofibrate may be helpful.

The rare type V hyperlipoproteinemia is often difficult to help in that correction of chylomicronemia requires restriction of dietary fat and correction of the prebeta lipoprotein increase requires reduction of carbohydrates. The necessary high protein diet is expensive and difficult to maintain. Reduction to ideal weight is often helpful. As for other forms of hypertriglyceridema alcohol should be restricted. Finally, progestational analogues may be useful.

Correction of the lipoproteinemia can bring distinct clinical benefit in 4 out of the 5 familial disorders. Fat free diet in type I stops recurrent attacks of abdominal pain, sometimes associated with overt pancreatitis. The liver and spleen become smaller and the eruptive xanthomas disappear. The three fold attack on type II hyperliproteinemia produces regression within a few months of tubo eruptive and planar xanthomas. Patients often report improvement in angina and intermittent claudication as the impaired peripheral blood flow improves. These observations constitute the first objective evidence of regression of human arterial lesions after correction of hyperlipoproteinemia. In type IV the occasional eruptive xanthomas are prevented and similarly in type V in which the clinical features resembling those of type I are also improved.

One large question that remains to be answered is does the restoration of normal lipid in type II or type IV lead to regression of established vascular disease or more hopefully to the prevention of vascular disease. Since there is a genetic basis of these disorders it means that the recognition of a case in a family can lead to the identification of more candidates for treatment often when they are young and free of symptoms.—L.H.N.

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Paroxysmal Atrial Tachycardia

Cardiac catheterization especially if the catheter is passed through the femoral vein, permits easy access to the His's bundle. Recording electrograms from the His's bundle reveals the initiation of depolarization of this structure. If this record is taken simultaneously with the surface electrocardiogram then A. V. conduction can be divided into 2 sequences. The first is P-H and the second is H-Q. The first approximates 80-140 m sec and reflects transmission within the ventricular conduction tissue. These two events together represent the interval between atrial and ventricular depolarization.

Recording from the His's bundles has clarified many of the mysteries associated with cardiac arrhythmias and conduction defects. One arrhythmia's mechanism, that of paroxysmal atrial tachycardia (PAT) especially has been clarified and with it logical ways to control it. All investigators have recognized the clinical association of atrial premature beats with PAT. One view held this tachycardia resulted from a rapid repetitive ectopic automatic focus. French authorities have long held that atrial premature beats might initiate PAT through a re-entrant mechanism. Recent studies by Goldreger and Bigger have proved the French view to be right and that PAT results almost always from retrograde atrial re-entry via the A. V. node which starts a reciprocating tachycardia.

They observed that PAT was always initiated by early atrial premature beats which arrived at the A. V. node during its relative refractory period with conduction delay. They showed furthermore that PAT could be terminated by single atrial premature beats which made the re-entry pathway refractory. Recording the intra atrial electrogram revealed that atrial depolarization normally proceeds from high to low atrium, but in the reverse direction during PAT. In over 100 patients without PAT the introduction by a pacing catheter electrode of progressively premature atrial depolarization during sinus rhythm never precipitated PAT. The opposite was true in 13 patients with a history of PAT. All these developed PAT with appropriately timed atrial premature contraction.

PAT is well known to occur in the various types of ventricular pre-excitation. Electrograms of the His's bundle have been used by Castellanos, et al to identify two distinct types of accessory A. V. communication, the bundle of Kent and of Mahaim in patients with Wolff-Parkinson-White syndrome (WPW). The setting up of a circus movement for a reciprocating tachycardia in these patients is easy to understand and in that case the tachycardia would resemble either a supraventricular or a ventricular mechanism depending on whether the circus movement moved antegrade through the normal A. V. conduction route or through a bypass.

In the WPW syndrome, tachycardia requires both pathways to be intact for the initiation and perpetuation of the tachycardia. Ligation of either the A. V. node or the accessory pathway can permanently prevent recurrent tachycardia. Recently Dreyfus, et al[12] studied the onset of ventricular fibrillation in one such patient. They suggested that the onset of atrial fibrillation with passages of impulses through the accessory fibers at a rapid frequency might reach the ventricles during the vulnerable period of excitability and thus account for sudden death in this syndrome.

Luria recently reported on a prospective study of the precipitating factors and associations of PAT in 120 patients seen over a period of 5 years. No associated abnormality was evident in 85 patients, 15 had a short P.R. when in sinus rhythm and another 14 had coronary artery disease. Recurrent PAT was the main symptom of primary disease of the heart muscle in 4 patients. A well known association in a minority of patients with cardiomyopathy and 2 had rheumatic heart disease. The tachycardias were remarkably benign. Only 4 of the patients died in the 5 years of whom 3 had evidence of coronary artery disease.

PAT might theoretically be prevented by drugs which depress automaticity such as lidocaine, quinidine or procainamide. Digitalis and propranolol prolong H-V conduction and thereby block re-entry. What does one do if these fail? One might then switch to a drug which enhances atrioventricular conduction thus removing the essential contribution for reciprocating tachycardia such as dilantin rather than trying another drug with the same mode of action that has already failed.

Propranolol is particularly appropriate for prophylaxis and treatment of PAT complicated by angina, precipitated by emotional causes or associated with thyrotoxicosis. Cardioversion should be avoided as hazardous in fully digitalized patients with drug resistant atrial tachycardia even though the need to restore sinus rhythm may be urgent. In such patients the right atrial wall can be electrically stimulated with a pacing catheter to "overdrive" the arrhythmia. An advantage of this method is that the electrode can be left temporarily in sites for the control of recurrences.—L.H.N.

Viruses In Lupus Erythematosus

Interest in the possible role of viruses in producing multi-system disease received its stimulus from two animal diseases, New Zealand Black disease in hybrid mice and Aleutian mink disease. Both of these have features in common with the connective tissue diseases particularly lupus erythematous (L.E.). There are also other animal diseases of viral etiology such as non-leukemic viruses causing renal disease in mice. There are also virus multisystem diseases in man. One is polyarteritis nodosa. Renal abnormalities have been described with various systemic viral infections.[1] Another reason for interest in the role of viruses in the connective tissue diseases has been the observation of myovirus like endothelial cell inclusions in the patient with systemic L.E.

In systemic L.E. there is present anti-DNA antibody, anti-double stranded RNA antibody and other antibodies in the serum. There is also present endothelial cytoplasmic inclusions in the glomerulus and other tissues and a probable depression of cellular immunity. There is unfortunately a moderate over-all elevation of antibody titer to a variety of viruses. These same phenomena have been observed in the animal models noted above in which viral etiology has been established. We can, therefore, reasonably consider the possibility that systemic L.E. patients like their animal counterparts also have a persistent viral infection that is responsible for the abnormal immune responses associated with this disease.

It is known that viruses can influence numerous variables of the immune response including antibody productions, immunoglobulin levels induction of immunological tolerance and various aspects of the cellular immune response.[2,3] Virus infection could lead to a depression of cellular immunity either through thymic injury which has been described in L.E.[4,5] or through the appropriation of thymus derived lymphocytes which are believed to be necessary for antigen. Depression of cellular immunity which has been found in several viruses in various species could in turn lead to even more widespread or diverse viral infection.

Persistent viral infection in systemic L.E. could have an adjuvant effect on the humoral antibody response at least to certain antigens such as the nucleic acid antigens[4] at the same time that it reduced cellular immunity. The LDN virus is an example of a virus that may stimulate serum antibody formation while depressing cellular immunity. In the case of the Epstein-Barr virus an interesting synergism between virus and antigen in the stimulation of an immune response has recently been described.[7] This is known as the adjuvant-like effect in which the virus together with another agent such as P.P.D. will lead to permanent immunoglobulin production. The viral infection could produce this "adjuvant-like" effect by stimulating lymphoid proliferation and by also making nucleic acid available through tissue breakdown. A viral adjuvant effect of the type proposed may also bring about absorption of tolerance to other auto-antigens that is such a striking feature of system L.E. Thus, loss of tolerance to auto-antigens has frequently been observed in experimental auto-immune diseases such as orchitis, thyroiditis and allergic encephalomyetitis when they have been experimentally induced by administration of the auto-antigen in Freund's adjuvant.

It is of interest that infectious mononucleosis believed to be caused by an infection with Epstein-Barr virus is associated with several serologic changes that also occur in lupus, such as positive antinuclear reactions, mixed cryoglobulins and the Rh. factor. In post-perfusion cytomegalo virus infection, an atypical mononucleosis-like illness occurring after cardiopulmonary by-pass or blood transfusions, various immuniological abnormalities have also been documented including erythrocyte autoantibody, Rh. factor, anti-nuclear antibodies, cold agglutinins and platelet and lymphocyte autoantibodies.

These autoantibodies have also been frequently identified in systemic L.E. Thus both Epstein-Barr virus and cytomegalo virus infections provide clinical examples of a type of influence that viruses can exert on the immunological responsiveness of the patient which appears to predispose him to the development of an "anto-immune disease."

With knowledge of the viral etiology of autoimmune disease we need but to search for an appropriate antibiotic against viral infections to eliminate these dread diseases.—L.H.N.

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Science Tools: In-Vivo Measurement Of Bone Mass By Photon Beam

Standard roentgenograms can only show changes in bone mass greater than 30 percent. For this reason it is not a good method of determining early osteoporosis nor its course. Clearly the clinical investigator and also the practicing physician needs an accurate method of measuring bone mass when one considers that osteoporosis is the largest single disorder of man.

In 1966, Cameron and Sorenson[1] presented a new method in which the X-ray beam is replaced by a monochromatic photon source. The method is quite reproducible in the same individual and the accuracy of direct photon absorption technique as determined by scanning cadaver forearms and measuring bone weight has been reported to be 4-7 percent. Goldsmith et al[2] have also provided evidence that the middle and distal portions of the radius examined by the photon absorption technique and the middle phalanx of the little finger examined by roentgenography were the sites and methods most likely to reflect the presence of osteoporosis of the spine.

Smith and Johnson[3] now report measurements of bone mass on 169 white women older than 50 were divided into 2 groups; those with (56) and those without collapsed vertebrae. In a group of normal women cortical bone mass varies directly with the width of bone. A width measurement is obtained from the scan. The scans were made over a site of predominently trabecular bone, one-tenth of forearm length and over a site of cortical bone, one-third of forearm length from the distal radius. Four scans are made at each site after which the average bone mass content and bone width were computed for each.

For the group as a whole it was assumed that patients with demineralization would have an increased incidence of vertebral collapse. It turned out that the difference in radial bone mass values is highly significant for both cortical and trabecular bone. This, of course, indicates that mineral loss from vertebra is reflected in the radius. There is clinical evidence for this concept. Iskrant and Smith reported the radius to be one of the sites with the highest incidence of fracture associated with vertebral osteoporosis.

In the fracture group there appeared to be a greater loss of bone mineral from trabecular than from cortical bone and the rate of bone loss vs. age appeared to be greater in trabecular than in cortical bone. The vertebra are trabecular bone so is the distal radius and it is not surprising that Smith's data should support the use of a scan of the distal radius to better reflect loss of bone mass in the vertebra.

There appears to be an equal rate of bone loss with age both in fracture and non-fractured groups. Thus, the osteoporotic individuals may simply be the persons who have the smaller skeletal mass in the normally distributed population over age 50 and as a consequence of the loss of mineral with aging they become susceptible to fracture earlier. A prospective study is needed to further evaluate this hypothesis.

The photon absorption technique appears to be a reproducible and accurate method for measuring bone mass in vivo and may be especially useful in observing an individual patient for a period of time. The method is capable of providing objective reproducible measurements of bone mass in man and this appears to be a promising tool for the study of the natural history of diseases of demineralization and of providing data on the response to treatment. It is especially needed at this time when we are on the threshold of reversing demineralization with such drugs as calcitonin.[4]—L.H.N.

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The Choice of Systemic Antimicrobial Drugs

(*Note*: This special issue of The Medical Letter brings up to date both text and tables on the choice of antimicrobial drugs in the October 4, 1968 issue [Vol. 10, p. 77]. Several new antimicrobial agents and revised indications for older agents are included in this revision. The tables on the choice of antimicrobial drugs begin on page 39.)

For each pathogenic organism there is generally one drug, or occasionally a combination of drugs, that is likely to be a better choice than other drugs or combinations. When the patient does not respond to a first-choice drug or cannot tolerate it, there is usually a preferred order of choice among alternative drugs. For each organism, therefore, the accompanying table lists first-choice drugs and alternative drugs in order of preference.

IDENTIFICATION OF THE ORGANISM—In choosing an antimicrobial drug, the physician must identify, at least tentatively, the organism responsible for the infection. The experienced clinician can often correctly identify or classify the organism on the basis of clinical evidence. A Gram stain of sputum, urine, wound exudate, or spinal fluid often yields a clue to the identity of the infecting organism and aids in the choice of a drug, at least for initial therapy before identification of the organism by culture. In most infections requiring antimicrobial therapy, smears and cultures are necessary.

The physician can do Gram stains and simple cultures in his own office; but whether he does tests himself or entrusts them to a laboratory, he should interpret the results with caution if they appear to conflict with the clinical evidence. Caution is especially necessary in interpreting the results of cultures from the upper respiratory tract. Such cultures may contain Haemophilus influenzae or pneumococci even when other organisms are responsible for the infection. The relative number of organisms may sometimes be helpful. When an organism is the only one isolated, or is predominant, or is present in large numbers, it is likely to be the cause of the illness; but even then, the exercise of clinical judgment is essential in interpreting the laboratory findings.

SUSCEPTIBILITY TESTS—*In vitro* tests of the susceptibility of an organism to various antimicrobial agents are especially useful with organisms notorious for their inherent or developing resistance, such as Staphylococcus, Enterobacter, Klebsiella, Proteus, Pseudomonas, and Escherichia coli. The Kirby-Bauer disc-sensitivity method is now preferred for routine studies, but it is not reliable for enterococci. An agent found active in susceptibility tests may prove ineffective if dosage is inadequate, if an organism other than the one responsible for the infection was isolated, if host resistance to infection is poor, or if abscesses or empyemas are present. Occasionally, an antimicrobial agent that is relatively inactive *in vitro* may be effective clinically;

soluble sulfonamides, for example, can provide effective concentrations in the urine although they may appear inactive in routine susceptibility tests. Even when an agent is very active *in vitro*, if the infection does not respond with reasonable rapidity, another drug should be substituted for it.

INITIAL TREATMENT OF SERIOUS INFECTIONS—In such serious infections as meningitis, gram-negative bacillary sepsis, and endocarditis, prompt treatment is essential and should not be withheld until laboratory studies are completed. Parenteral administration, preferably intravenous, is usually mandatory if an infection is severe. After the infection appears to be under control, an oral formulation can be used for maintenance therapy.

Meningitis — Ampicillin is effective against many of the organisms responsible for bacterial meningitis (pneumococcus, Haemophilus influenzae, meningococcus); for children more than two months of age, large doses (up to 400 mg/kg/day intravenously) are recommended for initial treatment before the results of laboratory studies are known. Since meningitis in adults is rarely due to Haemophilus influenzae, intravenous administration of large doses of aqueous penicillin G is recommended, pending the results of cultures. If culture of the spinal fluid shows that the organism is a meningococcus, pneumococcus, beta-hemolytic streptococcus, or non-penicillinase-producing staphylococcus, either penicillin G or ampicillin should be effective. For H. influenzae, most consultants prefer ampicillin in large doses, with chloramphenicol as an alternative.

Patients with meningitis who have histories of allergy to penicillin present a special problem. Some Medical Letter consultants would still treat such patients with penicillin if they have never had immediate reactions to it; but such patients must be observed closely and the physician must be prepared to treat anaphylaxis promptly (Medical Letter, Vol. 10, p. 101, 1968). Where the use of a penicillin seems unwise, a combination of chloramphenicol and erythromycin is recommended for initial therapy; if the culture yields pneumococci or meningococci, this combination can be continued.

In infants under two months of age, and especially in the immediate neonatal period, gram-negative enteric organisms are frequently responsible for meningitis, and many pediatric consultants recommend a combination of ampicillin with either kanamycin or gentamicin pending the results of laboratory tests. At any age, if the infecting organism is likely to be or proves to be Pseudomonas, most Medical Letter consultants favor the concurrent intravenous administration of 500 mg/kg/day of carbenicillin and 5 mg/kg/day of gentamicin. (For infants, the dose of gentamicin should be 6 mg/kg/day.) Some consultants would also give gentamicin intrathecally in single daily doses of up to 5 mg for adults and 1 mg for infants.

Reprinted from *The Medical Letter on Drugs and Therapeutics*, New York, N.Y., Vol. 13, No. 10, May 14, 1971.

Science News

Specialization And Technology Ad Lib

On March 23, Washington, D.C. Hospital Center opened a seven unit wing specializing in coronary, medical, surgical, renal, respiratory, burn and psychiatric intensive care.

The CCU has a master monitoring console capable of providing continuing or emergency monitoring of patients from other areas of the hospital and other hospitals. Through the use of data phones the ECG from a patient may be sent from another hospital to the central station where it can be displayed and observed for arrhythmias on a true tune basis. In addition, through the use of telecopiers previously recorded ECG's can be sent over the telephone lines to provide added information of consultative services concerning a particular patient.

So with renal and respiratory units.

So with acute pre-operative and post-operative surgical diseases.

Severe trauma patients with shock of varying etiologies, post-open heart surgery patients, organ transplants.

A special burn unit has its own treatment area for dressing changes and debridement. Hydrotherapy will also be a feature of the self-contained unit.

Concern for the emotional as well as the physical well being of patients will be shown by input from the department of psychiatry in every practice.

This approach will combine recent technological advances in monitoring and communications with a medical and nursing staff thoroughly equipped to enchance total intensive care.—L.H.N.

SUMMARY OF PROCEEDINGS
HOUSE OF DELEGATES — ANNUAL MEETING
Hartford, Connecticut — April 25, 1972

Reports and Addresses

The House received reports, addresses and/or remarks from the President, the AMA Delegates, the Secretary, the Treasurer, the Council, the President of the Woman's Auxiliary to CSMS, COMPAC and a number of delegates from other state medical societies. At luncheon, the members and guests of the House were addressed by Dr. Russell B. Roth, Erie, Pa., Speaker of the House of Delegates of the American Medical Association. The address of President Frederick C. Weber, Jr., Greenwich, is published at the end of this summary.

Election of Officers and Committees

With minor amendment, the House voted to approve the published report of the Nominating Committee (the Council). CSMS officers elected were:

President: David A. Grendon, Sharon
President-Elect: Sidney L. Cramer, Hartford
Vice-President: James H. Root, Jr., Waterbury
Secretary: Louis C. Backhus, Waterbury
Treasurer: Hilliard Spitz, New London
Speaker of the House of Delegates:
  Kenneth F. Brandon, Hartford
Vice-Speaker: Timothy F. Nolan, Greenwich
Two Delegates and Two Alternates to the American Medical Association—for the term January 1, 1973 to December 31, 1974.
  J. Alfred Fabro, Torrington (D)
  Morris A. Granoff, New Haven (A)
  E. Tremain Bradley, Norwalk (D)
  Sidney L. Cramer, Hartford (A)
Councilor-at-Large: Frederick C. Weber, Jr., Greenwich

Presentations and Awards

Presentation to Retiring President: In recognition of his untiring efforts on behalf of the Society and its members during 1971-72, Frederick C. Weber, Jr., Greenwich, received an engraved silver bowl and a past president's pin. This presentation was made by Kenneth F. Brandon, Hartford, Speaker of the House.

Presentation to Incoming President: At the Annual Dinner on Wednesday, April 26, an engraved gavel, symbolic of the office of President, was presented to David A. Grendon, Sharon, by Frederick C. Weber, Jr., Greenwich. Dr. Weber also administered the oath of office to the incoming President. Dr. Grendon's inaugural address is published at the end of this summary of proceedings.

AMA-ERF Grants: Provided by the American Medical Association's Education and Research Foundation, unrestricted grants were awarded as follows:

To the Yale University School of Medicine—$4,460. Accepted for YUSM by Arthur Ebbert, Jr., New Haven, Associate Dean.

To the University of Connecticut School of Medicine—$3,844. Accepted for UCSM by Robert U. Massey, Dean.

Service Recognition Award: A certificate for service to the Society was presented to Oliver L. Stringfield, Stamford, "in recognition of his personal initiative in developing and implementing an effective educational program on the subject of venereal disease for the students and faculties of the secondary schools in his community area, pursuant to the recommendation of the House of Delegates".

Presentation to the Society: On behalf of the Society, President Weber accepted with thanks from Pfizer Pharmaceuticals, Inc. a fifteen volume library on drug abuse. The library will be housed in the CSMS headquarters building in New Haven and will be available for use by all interested members.

Principal Actions Taken

Continuing the procedure established several years ago, all business coming before the House was heard by Reference Committees. Receiving the reports of the five Reference Committees, the House took actions as follows:

Report of Reference Committee No. 1

The House of Delegates acted on a series of reports of Reference Committee No. 1 as follows:

(a) *Resolution, J. Alfred Fabro, Torrington—Subject: Distribution of "Proceedings"*, AMA House of Delegates.

Voted to accept the recommendations of the Reference Committee on this resolution as follows:

(1) That published copies of the "Proceedings" of the AMA House of Delegates (for the Nov.-Dec., 1971 and June, 1972 meetings) be obtained and distributed to the members of the CSMS Council and to the secretaries of the component County Medical Association, and that the value of this program be assessed at the 1972 semi-annual meeting of the CSMS House of Delegates and a decision made as to the desirability of continuing it. The original resolution called for such distribution to be made to all members of the CSMS House of Delegates.

(2) That the Connecticut AMA Delegates prepare and submit a summary report on each meeting of the AMA House of Delegates to the first subsequent meeting of the CSMS House of Delegates.

(b) *Resolution, HCMA Board of Directors—Subject: Poll on "Connecticut Medicine"*

Voted to accept the recommendation of the Reference Committee that this resolution *not* be adopted. The resolution called for a poll to be made of the membership on the question of whether publication of the Journal should be continued. In conjunction with discussion of the resolution, the House was reminded of the results of a 1965 membership poll which indicated that two out of three members read the Journal "regularly or frequently"; rated the scientific articles as "excellent or good"; rated the non-scientific material (Council minutes, etc.) as "informative"; and rated the Journal third (to *JAMA* and the *N.E. Journal of Medicine*) in their preference for medical publications.

(c) *Resolution, HCMA Board of Directors—Subject: Catastrophic Coverage*

Voted to accept the recommendation of the Reference Committee that this resolution be adopted, as amended, as follows:

RESOLVED: That the House of Delegates of CSMS, through Connecticut's AMA delegation, urge the House of Delegates of the AMA to support legislation that will provide as much catastrophic health care coverage as possible through both the private and public sectors, and that this resolution, in suitably edited form, be transmitted to the June meeting of the AMA House of Delegates in San Francisco.

(d) *Resolution, HCMA Board of Directors—Subject: Specific Fee Schedule*

Voted *not* to accept the recommendation of the Reference Committee that this resolution be referred to the Committee on Third Party Payments for study and report to the Council; further voted *not* to adopt the resolution as submitted by the HCMA Board of Directors. *N.B.*: The resolution called for the Society to adopt a specific (statewide) fee schedule. The results of recent County Association surveys indicated a 4:1 member preference for "usual, customary and reasonable charges" vs. "fee schedules" as the basis of third party payment for physicians' services.

(e) *Supplementary Report—Committee on Organ and Tissue Transfers*

(1) *Resolution on New Connecticut Blood Program Facility*: Voted to accept the recommendation of the Reference Committee, as amended, that a subject resolution be adopted as follows:

RESOLVED: That the House of Delegates of the Connecticut State Medical Society endorse the plan of the American Red Cross to construct a new facility on the campus of the University of Connecticut Health Center at Farmington, and urge all physicians and all other citizens to participate generously in the $2.8 million building fund solicitations now under way in Connecticut.

(2) *Progress Report on Establishing Connecticut "Kidney Bank"*: Voted to accept the recommendation of the Reference Committee that the progress report filed by the Committee on Organ and Tissue Transfers on its study of the feasibility of establishing a "kidney bank" in Connecticut be received for filing (as information).

Report of Reference Committee No. 2

Subject: Reports of Committee on Continuing Medical Education re CME Program

The House of Delegates acted upon the subject report and recommendations of the Reference Committee as follows:

(1) Voted to accept the published annual report of the Committee on Continuing Medical Education for filing (as information).

(2) Voted to rescind two resolutions adopted by the House of Delegates on April 27, 1971 as follows:

RESOLVED: That the House of Delegates supports the concept of continuing medical education as a contingency of continuing membership in the Society and in the component County Medical Associations and proposes the development of a mechanism for the practical implementation of such concept, and that the implementation of this concept be the responsibility of the County Medical Associations, and be it further.

RESOLVED: That the House of Delegates charge the CSMS Committee on Postgraduate Education to develop and submit to the Council a system of CSMS-sponsored and/or CSMS-approved programs of continuing medical education designed to make practical the implementation of such concept as a primary responsibility of the County Medical Association.

(3) Voted to approve those portions of the reports (original and supplementary) of the Committee on Continuing Medical Education that had to do with developing CSMS sponsored and/or CSMS approved programs of CME for the membership within the state and at local level, and with accrediting such programs.

(4) Voted to delete those portions of the reports having to do with a CME-membership contingency with respect to CSMS and County Medical Association members.

(5) Voted to accept a substitute for the CME Committee's recommendation concerning CME and hospital staff appointments as follows:
"It is recommended that hospital medical staffs be encouraged to evaluate and implement the recommendation on continuing medical education proposed by the Joint Commission on Accreditation of Hospitals."

(6) Voted to accept the original and supplementary reports of the Committee on Continuing Medical Education as amended (above).

(7) Voted to instruct the staff of CSMS to edit the original report of the Committee on Continuing Medical Education to bring it into conformance with the amendments listed above under (3), (4) and (5). The report, as amended, follows:

Report of Committee on Continuing Medical Education

RESOLVED: That the House of Delegates support the concept of continuing medical education as a contingency of continuing membership in the Society and in the component County Medical Associations and propose the development of a mechanism for the practical implementation of such concept, and that the implementation of this concept be the responsibility of the County Medical Associations; and be it further

RESOLVED: That the House of Delegates charge the CSMS Committee on Postgraduate Education to develop and submit to the Council a system of CSMS-sponsored and/or CSMS-approved programs of continuing medical education designed to make practical the implementation of such concept as a primary responsibility of the County Medical Association.

At our Committee meeting on April 29, 1971, the above resolutions adopted by the House of Delegates on April 27, 1971, were discussed at length. Since that time a sub-committee and the committee as a whole has spent time attempting to evolve the best possible way of implementing the resolutions. Our deliberations have been guided by the questions submitted by the Council after its July, 1971, meeting, and by a more detailed analysis prepared by the Executive Director on the administrative considerations related to making CSMS membership contingent on evidence of continued medical education.

After due consideration it is the recommendation of the Committee that the Council recommend to the House of Delegates that it rescind the resolutions adopted in April, 1971, and now consider the attached plan for CME for the CSMS membership. This plan would more realistically reflect the objectives of continuing medical education for the Society's member physicians and for the medical profession as a whole.

Martin E. Gordon, M.D., *Chairman*

A Plan for CME for CSMS Membership

The Committee on Continuing Medical Education wishes to submit the following plan to involve the CSMS membership in continuing medical education. The plan attempts to take into consideration the various administrative details which prevent the Society from imposing an annual requirement of continuing medical education as a prerequisite for continued membership in the Society. The following plan encompasses a philosophy of continuing medical education and incorporates the use of the AMA's Physician's Recognition Award as a guideline for defining what can be accredited as continuing medical education.

Basic Philosophy Toward CME

Working within the philosophy of the State Medical Society, every physician should be motivated to improve his practice of medicine. The Society believes that every physician in Connecticut fulfills his obligation to himself and to his profession by committing himself to the principle of life-long continuing medical education. It is recommended that every physician in the state use as a basis for this commitment the minimum number of hours which are recommended by the physician's specialty, section or board.

In order to implement this basic philosophy, *Connecticut Medicine* will continue to publish events and programs in continuing medical education which are of interest to the physicians in the state. The Committee on CME will ask that county associations publicize local programs and that hospitals do the same.

Each county association will be invited to endorse this basic philosophy and will be encouraged to charge a committee on the local level to keep the membership aware of the need for CME.

The Committee on CME proposes to design a wallet-sized, calendar or daily reminder which each physician can keep an accumulative record of his activities in CME. This booklet can become the evidence necessary to fulfill any requirements expected of either his hospital, his county association, his section or specialty board of the AMA Physician's Recognition Award.

The estimated cost of this type of a calendar is not expected to be very great and it is possible that a pharmaceutical firm will be interested in financing the production costs. The calendar could include brief medical quotes, questions, mini-diagnoses, etc.

This basic philosophy toward CME will be kept in the forefront by publishing in Society periodicals any special recognition attained by members of the Society. Also, events like the Scientific Assembly will be featured among the programs of CME sponsored by the Society.

Implementation of Basic Society Philosophy of CME at the Local Level

Recognizing the fact that most CME takes place at the local hospital where a physician retains his staff privileges it is the intent of the Committee on CME that the medical staff at each hospital be encouraged to evaluate and implement the recommendation on continuing medical education proposed by the Joint Commission on Accreditation of Hospitals.

The Committee would inform hospital medical staffs of the Society endorsed philosophy on CME and would relate this philosophy to the principles of CME as they appear in the Manual of the Joint Commission on Accreditation of Hospitals.

In order to assist with CME activities at the hospital level, the Committee would assume the responsibility of accreditating CME programs offered at the hospital so that physicians would be able to utilize these programs for credits toward fulfilling the requirements possibly expected of him by his county association, his section or specialty board or for the AMA Physician's Recognition Award.

By surveying what hospitals are presently doing in the area of CME activities and by developing a set of guidelines for accreditation, the Committee believes that it will be able to develop a sound program of CME which will be readily available to the physician in a convenient and relevant situation. It is foreseen that this program, which is hospital based, could be opened to the physician who does not have staff privileges, thus making the program inclusive of all the community physicians who are responsible for the delivery of medical care to that particular locale.

AMA Award as a Guideline for CME Standards

Established in 1968, the AMA Physician's Recognition Award attempts to "accord recognition to physicians who participate regularly in continuing medical education . . ." The Award is granted for a minimum total of 150 credit hours of CME that are earned over a continuous three-year qualifying period. Application for the Award is open to all doctors of medicine in the United States without regard to citizenship or AMA membership.

The application form lists ten categories of CME activities which are creditable for the Award. Six categories are classified as required education; four are elective education. A credit hour is one hour of participation. The Award requires 60 credit hours in the required category and 90 credit hours in the elective category, a total of 150 in three years.

The Committee recommends that the Society encourage its members to apply for the AMA's Physician's Recognition Award.

By doing this, the Society would have to charge the Committee on CME to become the Society's accrediting agency for the local programs of CME. This would then make Connecticut physicians eligible for the Award which at present is technically available only to physicians who attended national, AMA accredited conferences or to those who teach, write, or are enrolled in a postgraduate degree program.

In becoming the designated agency the Committee, with adequate staff support, would accredit the programs of CME of local hospitals, programs in CME sponsored by county or city societies and programs sponsored by local units of voluntary health organizations.

The Society would assist in promoting this Award by sending information and applications to *all* Society members. Also, the Society would accord recognition where possible to members who have received the Award.

It would be possible to arrange with county associations and the American Academy of Family Practice for reciprocity with the Award for CME credits, thus avoiding duplication of effort on the part of Connecticut physicians.

Summary

The Committee on CME recommends that:

(1) The Council endorse the basic philosophy toward CME.
(2) The Council ask the counties to endorse the philosophy.
(3) The Council authorize the Committee on CME to become the accrediting agency for CME programs in the state.
(4) The Council encourage CSMS members to apply for the AMA Physician's Recognition Award.

The Committee on CME will:

(1) Publicize CME activities.
(2) Design a wallet-sized daily reminder, obtain estimates and report back to the Council on the actual expense or mode of financing.
(3) Recommend to hospital medical staffs evaluation and implementation of CME proposal of Joint Commission on Accreditation of Hospitals.
(4) Survey hospitals on present CME activities.
(5) Develop guidelines, in cooperation with the AMA, for accreditation of CME programs.

Report of Reference Committee No. 3

The House of Delegates acted on a report of Reference Committee No. 3 as follows: *Subject: Proposed CSMS "Connecticut Ambulatory Care Study"*

Voted to accept the subject report and recommendations of the Reference Committee as published herewith:

(1) That the report and recommendation of the Council on the Ambulatory Care Study and the resolution offered by the Committee on Statewide Medical Planning in its Supplementary Report be received for filing.
(2) That the House of Delegates approve the proposed Ambulatory Care Study to be carried out by the Connecticut State Medical Society, as outlined in the Supplementary Report of the Committee on Statewide Medical Planning.
(3) That the House of Delegates designate the Council as the fiscal and administrative agent of the Society for the Ambulatory Care Study, such designation to include responsibility for the terms and conditions of employment of all personnel engaged by the Society as staff for the Study, the disbursement of all funds received by the Society in connection with the Study, and the further development of plans leading to the filing of a grant request with HEW.

A substitute motion that would have rejected HEW funds and sought funds from other sources was lost (28-62).

It was voted to table a motion which would have authorized the Council to seek other sources for funds to finance the Study in the event that the grant presently anticipated from HEW fails to materialize.

Report of Reference Committee No. 4

The House of Delegates acted on a series of reports of Reference Committee No. 4 as follows:

(a) *Subject: Authorization to Form CSMS Section on Pulmonary Diseases*
Voted to accept the recommendation of the Reference Committee that authorization be granted to form a Section on Pulmonary Diseases.

(b) *Subject: Authorization to Form CSMS Section on Forensic Medicine*
Voted to accept the recommendation of the Reference Committee that authorization be granted to form a Section of Forensic Medicine.

(c) *Subject: Endorsement of Candidate for Vice-President, AMA*
Voted by acclamation to endorse the candidacy of Norman H. Gardner, East Hampton, for the office of Vice-President of the American Medical Association, 1972-73, as recommended by the Reference Committee and the Council.

(d) *Subject: Annual Report of Judicial Committee*
Voted to accept the report of the Reference Committee that the annual report of the Judicial Committee be accepted, and that the ques-

tion posed by the Judicial Committee in its report be referred to the Council for study and appropriate action; i.e., whether the Judicial Committee ought to initiate discussion and make recommendations concerning problems of medical ethics such as the donation of organs by minors, traditionally looked upon as legal and/or legislative problems, in consultation with representatives of other disciplines involved.

(e) *Subject: Educational Programs for Membership (NHCMA Board of Governors)*

Voted to accept the recommendation of the Reference Committee that a subject resolution be adopted as follows:

RESOLVED: That the House of Delegates of the CSMS encourage the County Medical Associations to hold Forums open to their membership for the purpose of discussion and consensus-seeking on the pros and cons of third party payor contracts; and be it further

RESOLVED: That these Forums be conducted well in advance of the closing dates for contract signings.

(f) *Subject: Revision of Connecticut's Abortion Statute*

Voted to accept the recommendation of the Reference Committee that the Supplementary Report of the Committee on State Legislation be accepted, and that a subject resolution introduced therein be adopted as follows.

RESOLVED: That the House of Delegates of the Connecticut State Medical Society reaffirm its policy on liberalization of Connecticut's abortion law, adopted by the House of Delegates on November 19, 1970, and direct that this policy be brought to the attention of the Governor, the Lieutenant Governor and the leadership of the General Assembly with the recommendation that, if the abortion statute is revised, it be revised in accordance with the subject policy of the Connecticut State Medical Society.

The stimulus for the supplementary report and resolution of the Committee on State Legislation was the recent ruling of a federal panel of judges that Connecticut's present stringent abortion statute is unconstitutional and the likelihood that the General Assembly may find it necessary to revise the abortion statute to conform with this ruling of the panel.

Report of Reference Committee No. 5

(a) *Resolution—Subject: Primary Entry of Patient Into Medical Care System*

The House voted to accept the report of the Reference Committee that a subject resolution be adopted as follows:

RESOLVED: That the House of Delegates of the Connecticut State Medical Society instruct all representatives of CSMS who serve on CRMP boards and committees to point out and pursue with vigor the concept that it is the considered opinion of the House of Delegates that the facility of the practicing physician is indeed the primary entry of patients into medical care and that this facility should be recognized as such.

(b) *Subject: Council-CRMP Representatives Communications*

It was voted to refer to the Council for study and appropriate action a "suggestion" of the Reference Committee that the Council inform CSMS members serving on CRMP boards and committees of actions taken by the Council concerning CRMP, and, in turn, to urge CSMS members serving on CRMP boards and committees to keep the Council posted on developments within their respective boards and committees.

Miscellaneous

Proposed Amendment to the Bylaws

Purpose: To combine the Committee on Accident Prevention with the Committee on Emergency Medical Services.

Action: The House voted to approve the combining of the named committees and to direct the Council to present to the 1972 semi-annual meeting an amendment to the Bylaws that will accomplish the stated purpose. (*N.B.*: The effect of this action is to place such an amendment to the Bylaws on the table for action at the 1972 semi-annual meeting, in accordance with the provisions of the Bylaws.)

Liaison with the State Welfare Department

It was voted to request the CSMS Council to continue efforts to establish liaison with the State Welfare Department.

ADDRESS OF THE PRESIDENT

Frederick C. Weber, Jr., Greenwich

At annual meetings of the House of Delegates, the outgoing President is expected to present a report to the House, and, as I undertake this duty, I appreciate the honor that befalls me. Viewed from this Society's highest elective office, a perspective of events, trends and inter-relationships comes into reasonably sharp focus and gives one an opportunity to look back critically on things that have happened—or not happened—during the past twelve months.

To review these happenings in detail is neither practical nor necessary in a report of this kind. Therefore, I will attempt only to interpret, from my own particular vantage point, the course that the Connecticut State Medical Society has been—and is—following in response to the demands of the times and the pressures being brought to bear on our profession by developments in a number of fields. As examples of the latter, I cite the increased emphasis being placed on the importance of continuing medical education and the politico-legislative pressures that are being exerted to restructure drastically our present American system of providing and financing health care services.

For some time various organizations have promoted the concept of reassessment examinations for physicians and this thought has been adopted and pursued by many state societies, several of which have recently instituted requirements for continued medical education as a condition of membership. One year ago, this House adopted that concept in principle. Since that time, the Committee on Continuing Medical Education has been working diligently to develop a program that would enable us to put our principle into practice, and has submitted a proposal for consideration at this meeting. During this same interval, the issue of continuing education has been taken up by legislators and incorporated into bills (not yet passed) which would regulate this activity by law rather than by our own design. Whether an improvement in the process would result from government intervention and enforcement seems highly doubtful. Nevertheless, the concept of continuing medical education has been made a matter of public concern and demands our most serious attention. If we sidestep the issue and fail to give it the attention it deserves, we stand to lose the right to do it our way.

For the past several years, medicine in general has undertaken quality and utilization review of physicians' services. We, in Connecticut, made an early start by monitoring the Medicaid program in 1967-69. This review process has now reached a very high level of sophistication in the case of some Foundations in which it plays a key role. Our Society has recognized the vital role to be played by peer review and has stressed its importance to the membership. Our Committee charged with this function has made singular progress during recent months and has reached the point where peer review is actually being performed for the Medicare B program, in cooperation with Connecticut General. Of special note is the fact that the direction this review is taking is toward *education* of the physician, with the objective of correcting deficient or aberrant practices by improving his *knowledge* of the standards of good medical practice.

The tie-in with the aforementioned efforts of the Committee on Continuing Medical Education is obvious. We now have two processes directed toward the same goal. It seems to me that the evolution of these efforts should ultimately produce a simplified system through which members of the Society could receive regular, recurring ses-

Speaker of the House Kenneth F. Brandon (right) presents Retiring President Frederick C. Weber, Jr., with an engraved silver bowl in appreciation for his untiring efforts on behalf of the Society and its members during his term of office in 1971-72.

sions of educational value in their local areas, monitored by their peers. The fruits of this experience would be readily apparent to local peer review committees which would then be better able to correct any individual or group deficiency by recommending specific changes in the educational program.

Advice, review, standardization, or appeal functions furnished by the County Association or the State Society could be adjusted to the needs as they became evident.

The convergence of the purposes of continuing education and improvement in quality of care through the direction our peer review efforts are taking, seems to me to assure that it will be merely a matter of time, further experience and improved organization before we can achieve our objectives in both areas.

It is proposed that the Society undertake a study of the office practice of medicine with respect to the quality and cost of care in this facility compared to that in group settings and in hospital clinics. This "Ambulatory Care Study" will be in the nature of a review of our method of rendering primary care to patients in our private offices and an assessment of its quality to see if we are meeting the standards of performance we are capable of attaining at a cost which compares favorably with methods others think may be preferable. This study will be an educational experience for those who participate, as it will give them a chance to judge themselves in relation to standards of quality, efficiency, and cost. The results should benefit the participants, the other practitioners, and the image of Connecticut medical care. Those who plan national health care programs may also be benefitted—perhaps more than anyone else—to learn where the majority of patients receive the best care.

The Society has passed a milestone this year with the establishment of a professional liability program in which the Society has a voice in the conditions of the contract, and also has a role in settlement of the cases. This marks a significant improvement in relations between the profession and the insurance industry. It marks an even greater step toward settling claims fairly by providing for a hearing to determine the merits of the claim and a means of settling the issue before long legal processes have become involved. Here again a start has been made in the direction of peer review and ultimately improved medical education.

In recent months we have begun to see instances where payments for hospital care under Medicare have been denied after the patient has left the hospital, on the basis that a certain period toward the end of his stay was not covered under new and ever-changing regulations. The hospital must then try to recover its bill from the patient who has been led to believe that his government-run Medicare insurance was "paying for his hospital care". He was not told that there was any likelihood of his stay being questioned on the basis of necessity for care. As a matter of fact, few patients have any concept of the time limits and exceptions imposed by Medicare on hospitalization. This arbitrary ruling, made known after the patient has left the hospital, occurs despite the efforts of hard working utilization and review committees in hospitals, whose members go over all extended stays carefully and pass judgment on their validity. Here we have a situation in which review by professionals is overruled by a third party which has limited knowledge of the situation and only arbitrary rules to go by. This is an example of the worst we can expect and also an example of where we must take a stand. We must have some representation and voice in the appeals mechanism. We must add this facet of our dealing with Medicare to our educational process and learn to forestall the possibility of arbitrary decisions by understanding the law, carefully documenting the need for continuing hospital stay, and justifying it before our local committee. Such pressure as this will make the Foundation concept, with responsibility for its own review, more attractive as a means of managing the care of patients by *our* rules.

This brings to mind the case in a nearby state where a judge found a doctor responsible for the entire hospital bill on the basis that admission was not medically necessary. Foundations have established certified hospital admission programs which would obviate any such ruling. A local hospital utilization and review committee as organized in Connecticut hospitals should be able to render a professional opinion on such a case and prevent it from getting to court.

Our educational process continues both in scientific developments and in economic areas. Under the circumstances, surrounded as we are by the third party payors, we must accommodate to the necessities of the times and keep up to date with rules and regulations as well as with Clinical Pharmacology and Drug Interaction.

Futhermore, we must remain *responsible* for patient care, whether in our office, or hospital, or extended care facility. There seems to be a tendency for others to claim *responsibility*. My understanding of the definition of that word allows only one interpretation, and that is that the doctor alone is responsible. The hospital, nursing home, etc. can only be held *accountable*. There is a difference and I think we should adhere to this distinction and not let the issue become confused by insurance, legislative, or administrative agencies.

This is my last opportunity to address you. It has been a great honor to have served as your President. I am most humbly grateful to the House of Delegates for my election. The understanding of the duties and responsibilities of the office has added to my feeling of appreciation for the confidence you entrusted in me a year ago.

I must thank our Executive Director and his able staff for providing needed help on innumerable occasions throughout the year. Without this wise counsel I could not have fulfilled the duties of this high office.

Your President-Elect, Dr. David A. Grendon, will be inaugurated at the annual dinner of the Society tomorrow night. Over the years that I have known him, I have become ever more impressed by his knowledge of our work, his sincerity of purpose and his integrity. I have confidence that the Society will be in good hands under his administration, and I assure him of my continuing support.

PRESIDENTIAL INAUGURAL ADDRESS

David A. Grendon, Sharon

It is indeed an honor for me to be addressing you as President of the Connecticut State Medical Society, for which I am most grateful.

The choice of a topic on an occasion such as this is difficult, not because there is so little to be said, but because we, as physicians, have for some time been rather depressed by what is happening about us, and to us. In his Shattuck Lecture in Boston last June, Dr. Himler referred to it as the "Anatomy of our Melancholy". We have become increasingly disturbed by the unkind and unfriendly criticisms leveled at us by the communications media. While some of this criticism may have been accurate and deserved, I grow weary of that tired old comparative statistic on infant mortality in this country as a proof of the poor quality of medical care, which has been worked to death, which never was valid, and which has been falling for some years. I grow weary of the characterization of organized medicine as a "union", since it has none of the attributes of unions as we know them. We are, in fact, fragmented and disorganized. We repeatedly hear the plea from our colleagues, 'Why don't we do something to improve our image?'. I, for one, am not convinced that a better public relations man, or a bigger advertising budget will solve our difficulties, much as tooth pastes or antacid tablets are sold. I am still young enough, and possibly naive enough, to believe that the best public relations gimmick at our disposal as individuals, is to be the best doctors we can be, with all that that implies, to be concerned with and considerate of our patients, and to continuously and for a lifetime improve ourselves as physicians.

We all know that our patients love us. Then why is there so much discontent with doctors in the abstract. To put the question in another form, what does society expect of medicine? Because the public is better informed on health matters than in the past, it is common knowledge that medicine has made tremendous advances, and the public wants to share in the benefits of those advances. If hearts are to be operated upon, cancer cured, organs transplanted, etc., people want these miracles to be available to them. But these are not

Outgoing President Frederick C. Weber, Jr., (left) presents President David A. Grendon with gavel at the Annual Dinner.

cheap miracles, hence the great involvement by planners, politicians and public, with devising systems which will bring the benefits of modern medicine within the reach of everyone, irrespective of economic status. But these are expensive services, and regardless of the system of delivery of health care, or how financed, it is self-evident that the more services rendered, the greater the cost. The playwright, Molnar told the story of several extremely wealthy men sitting around and discussing how they could go about dissipating their fortunes. One suggested by buying jewelry extravagantly, but with extreme wealth it would be impossible to put a significant dent in it in this way. Another suggested high living, but man's capacity for food and drink is limited. A third suggested expensive automobiles and boats, but great wealth can take these in stride. A quiet, slightly seedy man sitting nearby intruded, and said that he had been wealthy and was bankrupted by a thrifty wife, because the banks will accept all the money anyone cares to put in them. Health care is not unlike a thrifty wife, because it can absorb all the money society is willing to pour into it. Society wants better police protection, better housing, better education, better pollution control, for none of which it wants to pay. Society must decide how much it wants to pay for modern, sophisticated, expensive health care. Merely changing the system of health care delivery will not necessarily cut the costs nor improve or guarantee the quality of that care. Witness the financial difficulties of the Health Insurance Plan of New York. Witness the fact that for years the planners, such as Anne Somers, who opposed the dollar deterrent, deductibles and coinsurance in health care, have swung around 180 degrees and now advocate them as a means of cutting costs and discouraging overutilization. Witness the fact that millions of dollars are being poured into health maintenance organizations to keep them afloat. Witness the dissatisfactions of subscribers to prepaid plans with the kind of care that they get. Apparently the demands of society will not be met by a mere change in the delivery system. In the last analysis, the quality, cost and availability of health care depends not so much on the system of delivery, but on the motivation and integrity of the physicians involved. A prepaid group of twenty poor physicians, will not give as good quality care as a single good, dedicated fee-for-service physician.

But what do we, as physicians, as distinct from ordinary citizens, want from our health care system. Just as the public wants good health care, we, if we are worth our salt, want to practice good medicine. We have always, and more recently to a greater extent, sought to constantly continue to improve as physicians. We have always, and more recently to a greater extent, been concerned with the economic aspects of health care. Formerly this was expressed in the philanthropic free medical care in private office or free clinic. Now it expresses itself in terms of utilization or peer review, because while we may be physicians we are also citizens and subject to the same taxes as other citizens.

Are society's expectations really opposed to the expectations of doctors? I think not. Society expects good medical care. We want to give good medical care. It therefore becomes a problem of understanding the needs of society, the difficulties involved in meeting those needs and a willingness on the part of both parties to solve the enormously difficult details reasonably. Wild-eyed planners, and politicians with pie-in-the-sky revolutionary schemes for throwing out the baby with the bath-water, are raising false hopes and inflaming already irritated areas. Sloganeers who promote health maintenance or preventive medicine as if these were newly discovered concepts are not serving society well. And doctors who insist on holding the line, and can see neither need for nor reason to change by one iota, anything in the health care system, must be made to see the light. We may be good but we are certainly not perfect.

I would hope, therefore, that we as physicians, will become involved to a greater degree in the general concern with health care, on all levels, to advise and consent, when indicated. I would hope that we would, as rapidly as possible, build up effective peer review mechanisms, not only to meet government or society's demand for quality and cost control, but as an educational exercise and method of self-improvement. But most importantly, it is incumbent on organized medicine, if it is to effectively shape and influence the changes in direction which health care delivery will most certainly undergo in the immediate future, to become involved in and hopefully take a leadership role in the planning which must precede such changes. Holding the line would be an exercise in futility. We must as individuals and collectively go where the action is. Let's try it, we may like it!

April 26, 1972

FIFTY YEAR MEMBERS HONORED

Newly installed President Grendon and immediate past President Weber with honored guests who were recipients of fifty year membership pins and certificates: Drs. Frederick C. Weber, Jr., Greenwich; Wilmarth Bradford Walker, Cornwall; Winfield Emmons Wight, Thomaston; William Witter Wright, West Hartford; David A. Grendon, Sharon.

Three of the seven physicians honored by the Society as fifty year members were present at the Annual Dinner on April 26, 1972, at the Hilton Hotel in Hartford. Each physician was presented with a framed certificate and a fifty year pin by President Frederick C. Weber, Jr. As each recipient was introduced, Dr. Weber gave a brief statement on the individual's professional background.

Those present as honored guests were:

Wilmarth Brandford Walker, M.D., Cornwall; graduate of the Yale University School of Medicine, 1920; member of the Litchfield County Medical Association.

Winfield Emmons Wight, M.D., 24 Goodwin Ct., Thomaston; graduate of Bowdoin Medical School, 1920; member of the Litchfield County Medical Association.

William Witter Wright, M.D., 200 Fern Street, West Hartford; graduate of the Harvard School of Medicine, 1919; member of the Hartford County Medical Association.

The following were not able to attend the dinner, but will be presented their pins and certificates at a later date:

Freeman Pell Clason, M.D., 40 West Hill Drive, West Hartford; graduate of the Harvard School of Medicine, 1915; member of the Hartford County Medical Association.

Isidore Hendel, M.D., 50 State Street, New London; graduate of the Jefferson Medical School, 1917; member of the New London County Medical Association.

Maurice Manuel Hillman, M.D., 129 Whitney Avenue, New Haven; graduate of Columbia School of Medicine, 1919; member of New Haven County Medical Association.

Luther Kyner Musselman, M.D., Lt. River Lane, Old Lyme; graduate of Johns Hopkins School of Medicine, 1919; member of the New Haven County Medical Association.

Electrocardiogram of the Month:

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

The Significance of QT, QTc, QaT, and QaTc: concluded

I—Shortening of the QT interval with decrease in the QTc value. It will be recalled that the QT interval represents the duration of ventricular repolarization and QTc the value corrected for heart rate. A decrease in the value of QTc is indicative of accelerated repolarization. In clinical practice digitalis in sufficient concentration is a very common cause of such a finding in the electrocardiogram. Other causes of accelerated ventricular repolarization are fever, thyrotoxicosis, and stimulation of the sympathetic nerve supply of the heart.

Fig. A exhibits the typical effect of digitalis on the electrocardiogram. It is taken from a female, age 60, who had been digitalized because of the presence of acute congestive failure. The PR interval is slightly prolonged to 0.23 second. There is slight arc-like depression of the ST segments in leads 1 and aVL and slight arc-like elevation of the ST segments in leads aVR and VI. The R-R intervals measure 0.86 second. The QT interval measures 0.30 second. The QTc value is decreased to 0.33 (normal range 0.39 to 0.42).

II—Shortening of the QaT interval with decrease in the QaTc value. It will be recalled that the QaT interval is an indirect measure of the initial slow phase of ventricular repolarization and QaTc the value corrected for heart rate. A decrease in the value of QaTc represents acceleration of this early phase. The most common cause of a shortened QaT interval and a reduced QaTc value is an elevation of serum ionizable calcium.

Fig. B exhibits the typical effect of hypercalcemia on the electrocardiogram. The patient was a male, age 56, with multiple myeloma in whom the serum calcium level was found to be 19 M.eq./L. The patient had not received any digitalis. There is a sinus tachycardia of 135 to 140 beats per minute (R-R intervals of about 0.44 second), The QT interval measures approximately 0.16 second. The QaT interval, measured in those leads in which the T wave is monophasic, is approximately 0.10 second. The QTc value is decreased to 0.24 (normal range 0.39-0.42) and the QaTc value is reduced to 0.18 (normal range 0.28-0.33).

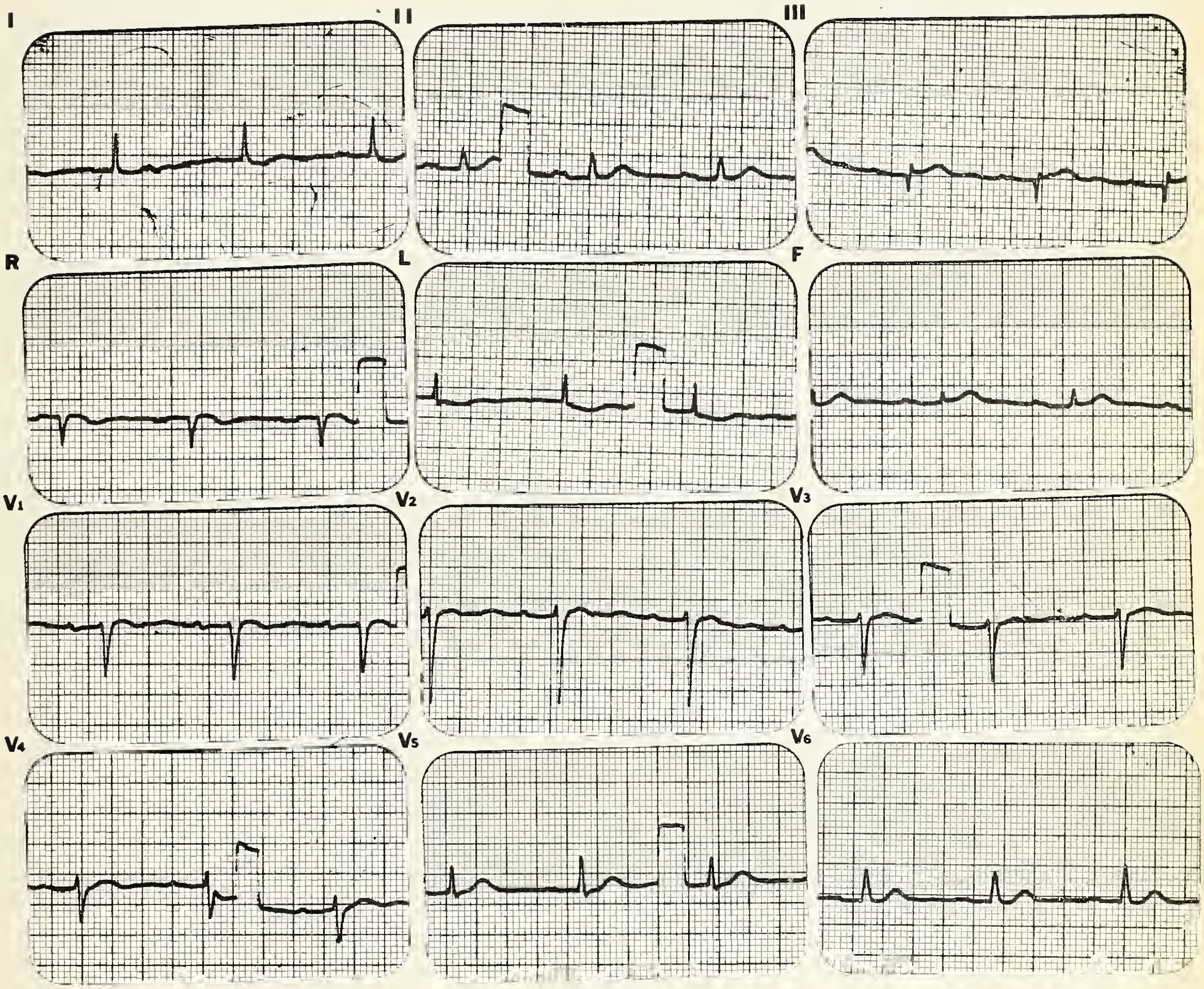

Figure A

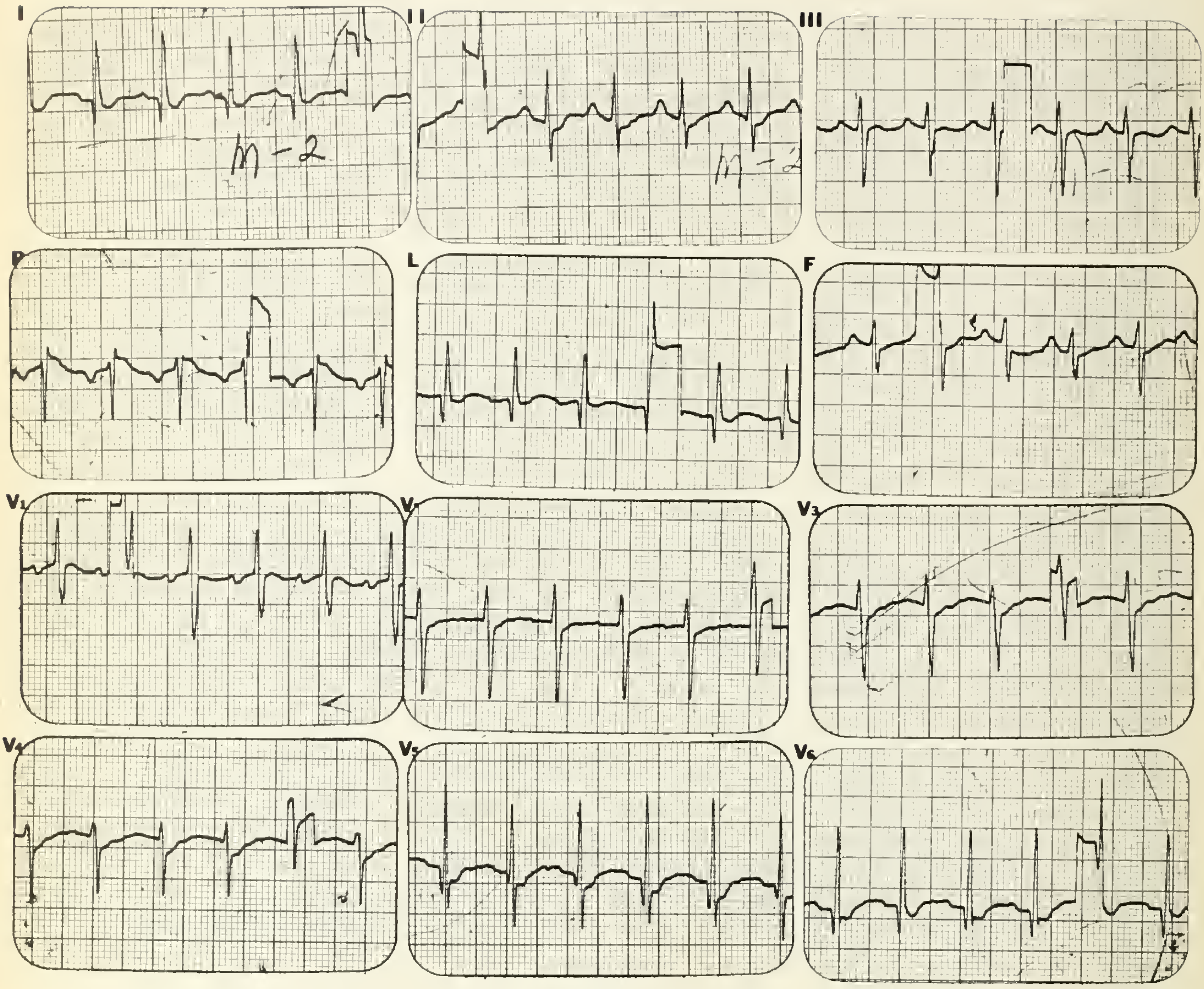

Figure B

...in the presence of spasm or hypermotility, gas distension and discomfort, **KINESED**® provides more complete relief:

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Contraindications: Hypersensitivity to barbiturates or belladonna alkaloids, glaucoma, advanced renal or hepatic disease.
Precautions: Administer with caution to patients with incipient glaucoma, bladder neck obstruction or urinary bladder atony. Prolonged use of barbiturates may be habit-forming.
Side effects: Blurred vision, dry mouth, dysuria, and other atropine-like side effects may occur at high doses, but are only rarely noted at recommended dosages.
Dosage: Adults: One or two tablets three or four times daily. Dosage can be adjusted depending on diagnosis and severity of symptoms. Children 2 to 12 years: One half or one tablet three or four times daily. Tablets may be chewed or swallowed with liquids.

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Allergist—Wanted as soon as possible. To join allergy practice in the southern part of the state. Large shore community.

Allergist—Opportunity in medium size community in Fairfield County. Convenient to New York

Allergist—To assume active private practice. Present allergist will remain to orient new physician. Conveniently located community. Drawing population of 200,000.

Anesthesiologist—Two board eligible or certified anesthesiologists needed in urban hospital in the central part of the state.

Anesthesiologist—Large urban hospital has vacancy. Located in western part of the state.

Anesthesiologist—To join three man group in 180 bed community hospital. Interest in inhalation therapy and respiratory physiology important. Recent or near future residency graduate acceptable. Living conditions excellent in semi-rural area with nearby University of Conn. and State College affording many recreational and cultural advantages. Please contact Anesthesia Associates, P.O. Box 23, Willimantic, Connecticut 06226. Tel. 423-9201.

Anesthesiologist—To join Board certified chief of anesthesiology in small community hospital. No OB. Salary negotiable. If interested contact administrator or chief of anesthesiology. Johnson Memorial Hospital, Stafford Springs, Connecticut 06076.

Anesthesiologist—Associate position in medium sized community. Centrally located.

Emergency Room Physician—To complete four-man group. 100-bed, full service hospital. Solid backup in all specialties and most subspecialties from Active Staff. Central Connecticut community midway between Hartford and New Haven. Must be eligible for Connecticut licensure. Attractive salary, excellent benefits. Resumé to Chief of Staff, World War II Memorial Hospital, Meriden, Connecticut 06450.

Family Practice—Two physicians seeking a third in attractive shore community. Busy summer practice. Hospital conveniently located. Send resume to Karl R. Friedman, M.D., Old Lyme, Connecticut 06371.

Family Practice—Practitioner needed in rural community in the western part of state. Physician in community willing to assist in establishing newcomer in rural, solo practice.

Family Practice—Suburb of New Haven has opportunity for an associate in family practice.

Family Practice—Physicians in community northwest of New Haven searching for additional practitioner. Small, up-to-date community hospital.

Family Practice—Practitioner wants to retire. Very attractive practice in southwestern Connecticut. Shore community. Near NYC.

Family Practice—Darien has ideal arrangement for newcomer. No OB. No surgery. Recently deceased physician had well established practice. Contact James V. MacGregor, M.D., 2 Queen Lane, Darien.

Family Practice—Two cities just north of Hartford in search for practitioners. Growing communities on Connecticut River. Physician Search Committees willing to assist newcomer with free office rent, etc.

Family Practice—North Branford, All America City, suburb of New Haven, requires family physician to establish practice. No other physician at this time. Contact Irving H. Beck, Town Manager.

Family Practice—Southwestern Litchfield County. Community hospital. Conveniently located. Community physicians also searching for pediatrician and Ob/Gyn to enter private practice.

Family Practice—Growing community seeks family physicians. North-central Connecticut. Approximately 47,000 population. Several hospitals in the area. New hospital in planning stages. Number of specialists in town. Conveniently located.

Family Practice—Full time or part time associate wanted for the shore community of Waterford, Connecticut. Busy summer practice. Community hospital readily available.

General Practice, Internal Medicine, Ob-Gyn and ENT: Needed in town of Torrington. 200 bed hospital. 50 physicians, over 50,000 population, Contact Joseph F. J. Curi, M.D., Chairman of Search Committee, Charlotte Hungerford Hospital, Torrington, Connecticut 06790. 203-482-0441.

General Practice and Internal Medicine—Both for solo and hospital based practice. Medium sized, north central community. Community hospital. Needed immediately.

General Medicine and Internal Medicine—Northwestern Connecticut community seeking to attract practitioners. Associate type practice possible.

Insurance company employee health service: Fulltime physician. Many employment exams and periodic physicals at Aetna suggest someone with strong diagnostic skills. Family practice or internal medicine preferred. Regular hours with weekends free. Retirement, medical and other company benefits. Salary up to $25,000. Send resume to E. S. Meinke, Personnel Department, Aetna Life and Casualty, Hartford, Connecticut 06115. An equal opportunity employer.

Internist—Community physicians seek additional internist to establish practice in medium size city northwest of New Haven.

Internist—Scenic northwestern community needs an internist. Physicians willing to assist candidate.

Internist—Interest in allergy, rheumatology or infectious diseases. Association with large clinic in central Connecticut.

Internist—Needed immediately to associate with large practice. Darien-Stamford area.

Internist—University setting. New facility. Ideal for proper candidate.

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Division of Beecham Inc. Bristol, Tennessee 37620

Internist—Northwest Connecticut prep school, good salary, excellent retirement benefits, family living, schools, recreation, large house, facilities for private patients, vacations. Help practice busy board certified FACP. 100 miles New York City, one hour Hartford, Albany. Curriculum vitae to: F. E. Smith, Jr., M.D., F.A.C.P. Salisbury, Connecticut 06068.

Internist—Rural community, but close enough for commute to Hartford. Small, community hospital. Physicians searching for additional coverage.

Internist—A third Internist is needed to join two other Internists in the town of Manchester, Connecticut. Office located across the street from a 300 bed community hospital which is currently in the second of a three stage building program. Manchester is located fifteen minutes from Hartford, one hour from New Haven, one hour and a half from Boston and two hours from New York City. For further information contact: Harold J. Lehmus, M.D., or David L. Warren, M.D., 56 Haynes Street, Manchester, Connecticut 06040. Telephone: 203-646-1167.

Internist—Preferably Board Certified or eligible, for chronic disease and cancer hospital having sections for TB in adults and children. 35 hr. week, 11 paid holidays, sick leave, 3 weeks vacation after one year of service. Salary level: $23,227-28,333. Paid health insurance and minimum charge for life insurance. Apartment available for physician with small family. Write Medical Director, Uncas-on-Thames Hospital, Norwich, Connecticut 06360.

Neurologist—Litchfield County area. Search Committee of the Medical Staff will assist qualified candidate.

Neurosurgeon—Opportunity in southwestern shore community. Near N.Y.C.

Ob/Gyn—Community in western Connecticut in search of physician to open private practice. Community's growth requires additional medical services.

Ob/Gyn—Associate needed. Attractive community. Short distance from Waterbury.

Ob/Gyn—Associate needed for Waterbury group.

Ob/Gyn—Fourth ob/gyn needed in southeastern Connecticut town.

Ophthalmologist—Three vacancies. Each in the larger cities of Connecticut. Immediate opportunities.

Ophthalmologist—Associate needed to join two other ophthalmologists in large, centrally located Connecticut city.

Orthopedics—Several opportunities for association with established specialty groups.

Otolaryngologist—Two physicians approaching retirement. Eastern part of the state. Coastal area.

Otolaryngologist—Central Litchfield County in search for specialist.

Pathologist—Needed to join staff of hospital in large southwestern shore community.

Pathologist—Chief of Pathology wanted for 100 bed, full service community hospital. Excellent lab facilities, well staffed and equipped. Fee for service or salary. Central Connecticut. 20 minutes to either Hartford or New Haven. Resumé to Chief of Staff, WW II Memorial Hospital, Meriden, Connecticut 06450.

Pathologist—Director of Pathology to direct laboratories at the William W. Backus Hospital, 326 Washington Street, Norwich, Connecticut 06360.

Pediatrician—Community physicians feel that another pediatrician is needed. Central section of the state. 40% of population 18 years of age and under.

Pediatrician—currently board-eligible or board certified. Full-time position. Salary negotiable. To practice family oriented medicine in a private, non-profit neighborhood health center. For further information please contact Evans H. Daniels, Jr., M.D., Medical Director, Community Health Services, Inc., 1023 Albany Avenue, Hartford, Connecticut, 06112. Telephone 549-1423.

Pediatrician—Needed to join physician in the Waterbury area.

Pediatrician—Community of Enfield needs pediatrician. Growing community north of Hartford.

Pediatrician—To join pediatrician in northeastern portion of the state.

Proctology—Lucrative practice available in New Haven. Physician deceased. Fully equipped office. Contact: A. M. Murray 203-787-4161.

Psychiatrists—Needed for state facility. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

Psychiatrists—Openings in mental hospitals and mental health clinics under the auspices of the State of Connecticut. Write Personnel Administrator, Department of Mental Health, 90 Washington Street, Hartford.

Psychiatrist—Board Certified or Eligible, to Direct Mental Health Clinic in General Hospital, half time, $15,000 to $25,000 depending on qualifications, opportunity for private practice, prefer with clinical experience and interest in development of comprehensive community services; attractive living in semirural community with University, near urban centers; send curriculum vitae with inquiry to Richard B. Ogrean, Administrator, Windham Community Hospital, Willimantic, Connecticut.

Radiologist—Needed immediately at Veterans Hospital. Contact Medical Director, Rocky Hill Veterans Hospital, Rocky Hill, Connecticut.

Radiologist—Small community hospital in northwestern part of the state needs a radiologist.

Radiologist—Large hospital needs radiologist.

Senior Physician—positions available at Norwich Hospital. Primary responsibility for medical care of geriatric and mentally ill patients in a community oriented, geographically unitized hospital with many forward looking, exciting programs. Starting salary $20,465, many fringe benefits, housing available. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

Surgery—General—Board certified surgeon seeking Board certified partner or associate in general surgery to practice in northern Connecticut. Small community hospital. Attractive community. Conveniently located. Write Physician Placement Service.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS' PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT

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Placement Wanted

The Placement Service has numerous resumes on file for physicians available for positions in Connecticut. Space does not permit printing individual advertisements. Anyone interested in resumes of candidates in the following specialities are asked to contact the Placement Service for more information (865-0587): allergy, anesthesiology, dermatology, family practice, internal medicine, neurology, neurosurgery, ob/gyn, ophthalmology, orthopedics, otolarynology, pathology, pediatrics, psychiatry, radiology, surgery, and urology.

Allied Personnel

Assistant or Associate Hospital Administrator—Medium sized hospital. Available Sept. 1972. Masters of Business Administration from Univ. of Florida, University Hospital of Jacksonville. 27 years of age. Married. Wishes to locate in Connecticut or Massachusetts. David B. Driggs, 1220 LeBaron Avenue, Jacksonville, Florida 32207.

EEG Technologist—31 years of age. Nine years of experience. Wishes position as instructor in clinical EEG Technology or technologist in charge of new laboratory. Available June 1. Presently at University of Kentucky completing degree program. Richard F. Wilmarth, 133 Brown Avenue, Lexington, Kentucky 40505.

Physician's Assistant—25 years of age. Presently enrolled P.A. Program at Duke University. Desires smaller coastal community. Assisting solo practitioner or group practice. David E. Lee, 2104 Chapel Hill Road, Durham, North Carolina 27707.

Physician's Assistant—30 years of age. Presently enrolled in Physician's Associate Program at Duke University. Available September 1972. Desires position with general practitioner, pediatrician or internist in solo or group practice. Ralph B. Lenoci, 261 King Street, Port Chester, New York 10573.

Business Manager—College graduate; 13 years administrative experience in clinic, hospital and health care fields. Available within 30 dasy. Irven V. Roberts, 85 Prescott Street, Torrington, Conn. 06790. 482-8398.

Physician's Associate—Special training in general surgery, urology, orthopedics and plastic surgery. Experience as a OR scrub technician. B.S. Degree. Will complete P.A. Program at Duke University in August. Patricia E. McNabb, 802 Louise Circle, Apt. 29-L, Durham, North Carolina 27705.

MEDIHC Program—Former military medics; number of candidates available. Contact: Henry J. Miller, Military Experience Directed into Health Careers, 640 Chapel Street, New Haven, Connecticut 06510. Phone: 865-0862 collect.

Summer Employment Wanted — Camp physicians; part time or vacation coverage. Medical students seeking hospital or laboratory positions. Contact: Connecticut State Medical Society—203-865-0587.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS' PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Pre-Sate®
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CAUTION: Federal law prohibits dispensing without prescription.

Indications: Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (*i.e.*, several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications: Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied: Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

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Pre-Sate® (chlorphentermine HCl)...the increasingly practical appetite suppressant

X-Ray of the Month

Section of Chest Diseases

The Natural History of Tuberculosis

Yale-New Haven Medical Center

Arnold B. Rilance, M.D., Director, Winchester Chest Clinics

M.T. was a 16 year old male admitted to the Yale-New Haven Hospital on 10/6/69.

Chief Complaint: Chest pain.

H.P.I.: In 1968, the patient was found to have a positive tuberculin reaction. During the next year a dull aching pain had been intermittently present in the right side of his chest. A non-productive cough had been noted. An X-ray of his chest taken on 10/6/69 revealed pleural reaction in the lower one-half of the right hemithorax that was considered due to a thin layer of encapsulated pleural effusion. In addition, there was evidence of enlargement of the paratracheal nodes at the level of the azygos node. The lung fields were clear.

Additional history: a 2 year old nephew had a positive tuberculin test. The patient's step-mother was under active treatment for pulmonary tuberculosis. An older sister subsequently developed active tuberculosis.

The patient was advised to accept chemotherapy for his tuberculosis but refused and was lost to follow-up.

On 3/29/71, the patient was readmitted to the hospital for treatment of an infection of the antecubital area secondary to the intravenous injection of heroin. Therapy for this infection was effective. An X-ray of his chest taken on 3/29/71

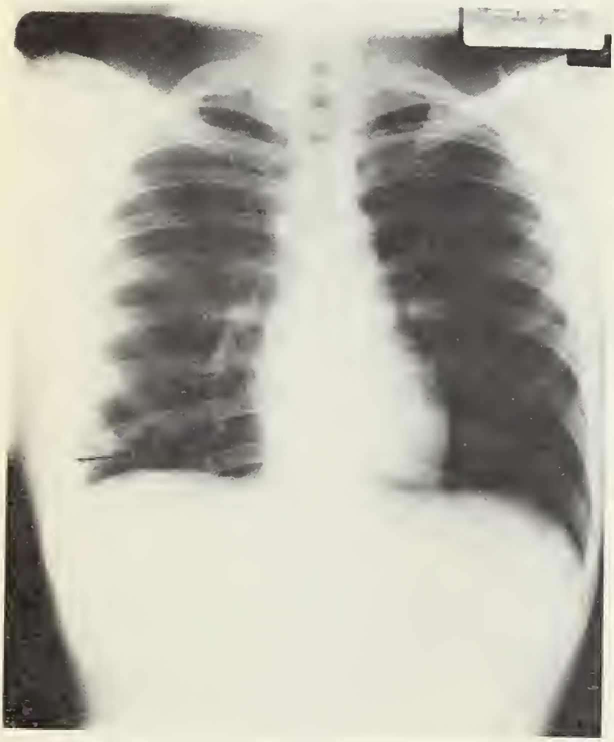

Figure 1

An X-ray of the chest, 10/6/69, reveals a thin layer of encapsulated effusion along the right lateral chest wall (lower arrow). In addition there is fullness in the right paratracheal area due to lymphadenopathy (upper arrow).

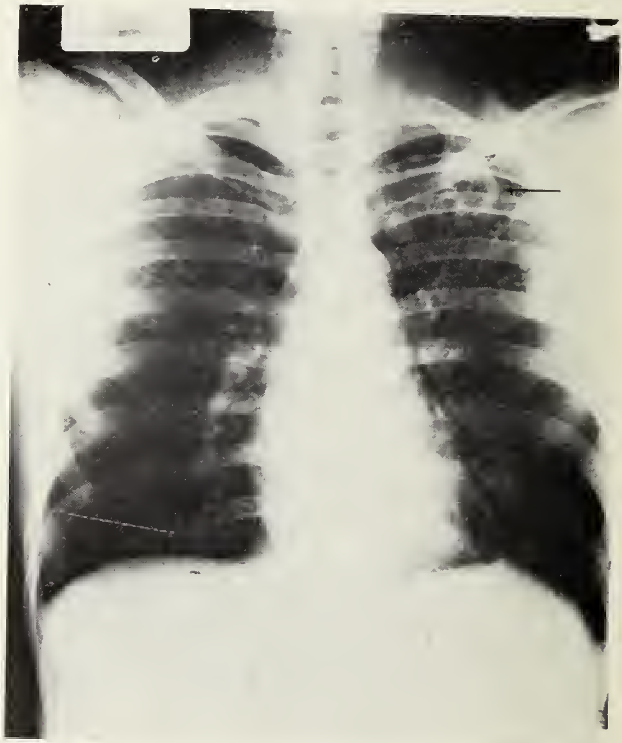

Figure 2

X-ray dated 3/29/71. Clearing of pleural effusion and paratracheal lymphadenopathy. However, there is a thin walled tuberculous cavity under the left clavicle with patchy infiltration at the periphery of the left 2nd and 3rd interspaces.

revealed clearing of the right sided effusion and paratracheal nodes noted in a film of 10/6/69, but a fresh thin walled cavity is to be seen under the left clavicle associated with tubercle bacilli in his sputum.

Comments: The course of events illustrated by this patient is characteristic of the slowly progressive nature of tuberculosis. The first stage of the disease is the development of a positive tuberculin test, frequently followed within the next two years by pleural effusion or tuberculous lymphadenopathy. These manifestations of the disease may be followed, as in this patient, at a later date, by the development of chronic active pulmonary tuberculosis.

Treatment at any stage prior to the development of pulmonary tuberculosis may eradicate the infection and minimize the degree of morbidity. It is for this reason that one year of prophylactic Isoniazid therapy in the treatment of young tuberculin reactors has become a generally accepted procedure. One could have hoped that prophylactic Isoniazid therapy in this patient when a positive tuberculin test was found might have prevented the subsequent development of his tuberculous pleurisy, mediastinal adenopathy and the cavitary tuberculosis in his lung.

SEROLOGIC TESTING

In April the Council of The Connecticut State Medical Society voted to accept as Society policy the following statement on routine serology as recommended by the Committee to Study Perinatal Morbidity and Mortality:

IN ADDITION TO THE INITIAL PRENATAL SEROLOGICAL TEST (FOR SYPHILIS) REQUIRED BY LAW, ALL EXPECTANT MOTHERS, ON BEING ADMITTED TO A HOSPITAL FOR DELIVERY, SHOULD HAVE BLOOD DRAWN FOR SEROLOGY (VDRL).

The above statement was evolved by the Committee over a period of several months after thorough discussion of all the issues involved. Also, the Committee under the chairmanship of Jacob Greenblatt, M.D., Stamford, had an opportunity to evaluate replies from twenty-nine of the thirty-two hospitals in the state, which were surveyed concerning their policy on routine serological testing.

Copies of this policy statement have been sent to the Commissioner of Health, the Maternal and Child Health Section of the State Department of Health, the Chief of Obstetrics and the Chief of Pediatrics in each hospital in the state and to the secretary of the Connecticut Society of American Board Obstetricians and Gynecologists.

OBITUARY

Thomas D. Murphy, M.D.
1900-1972

Dr. Thomas D. Murphy died March 29, 1972 at the Rutland Hospital, Rutland, Vermont.

He was graduated from Troy Conference Academy in Poultney, Vermont. He attended the University of Vermont for one year and finished his academic work at Catholic University of America, Washington, D.C. receiving an A.B. degree. In 1930 he received his M.D. from College of Physicians and Surgeons, Columbia University. He served his internship at Gallinger Hospital, Washington, D.C. and the Hospital of St. Raphael, New Haven. He did one year of postgraduate work in surgery at the University of Pennsylvania.

Dr. Murphy entered the general practice of medicine at Terryville, Connecticut and later moved to West Hartford.

In 1942 Dr. Murphy enlisted in the U.S. Navy and retired as Captain. He spent five years with UNRRA, most of which was in China. When he returned to the United States he entered the service of the U.S. Veterans Hospital. He practiced in Lowell, Massachusetts, Hartford, Connecticut and for the past eighteen years in Manchester, New Hampshire.

Dr. Murphy was a member of the American Medical Association, the Connecticut State Medical Society, the Hartford County Medical Society and Navy League of the United States.

Owen L. Murphy, M.D.

In Memoriam

Moss, **Harry G.**, New York University College of Medicine, 1928. Dr. Moss was a general practitioner in the New Haven area since 1946. During World War II he served as a Captain in the Medical Corps, U.S. Army. He was an associate in medicine at Yale-New Haven Hospital and on the courtesy staff of St. Raphael's Hospital. He was a member of the New Haven County Medical Association and the Connecticut State Medical Society. Dr. Moss died April 27, 1972, at the age of 66.

Meeting Notices

GENERAL

April 24, 25, 26, 1973
181st Annual Meeting of the Connecticut State Medical Society
Hartford

October 18—Wednesday (9:30 a.m.-4:00 p.m.)
"Multidisciplinary Approach to Patient Care"
Sheraton-Park Plaza, New Haven

CLINICAL IMMUNOLOGY AND ALLERGY

July 17-19—Monday-Wednesday
Current Concepts
Washington Plaza Hotel, Seattle, Washington

ELECTROENCEPHALOGRAPHY

October 9-11—Monday-Wednesday
Shamrock Hilton, Houston, Texas
Contact: D. W. Klass, M.D., Mayo Clinic, Rochester, Minn.

EXTRA-CORPOREAL TECHNOLOGY

July 27-29—Thursday-Saturday
Tenth International Conference
Waldorf-Astoria, New York City

INTERNAL MEDICINE

September 5-9—Tuesday-Saturday
International Society of Internal Medicine
Twelfth Biennial Congress
Boston, Massachusetts

OCCUPATIONAL HEALTH

September 11-12—Monday-Tuesday
32nd Annual AMA Congress on Occupational Health
Drake Hotel, Chicago, Illinois

PEDIATRICS

November 15—Wednesday
Fourth Biennial Perinatal Seminar
Connecticut General Auditorium
Bloomfield

PULMONARY PHYSIOLOGY

October 22-25—Sunday-Wednesday
Clinical Pulmonary Physiology
Poughkeepsie, New York
Contact: New York Trudeau Society, Room 710, 105 East 22nd Street, New York, New York 10010

WOMAN'S AUXILIARY

President
Mrs. Joseph C. Czarsty, Litchfield

President-Elect
Mrs. George Roch, Windham
First Vice-President
Mrs. A. W. Thomson, Jr., Middlesex
Second Vice-President
Mrs. David O'Keefe, Hartford

Recording Secretary
Mrs. Boris Rifkin, New Haven
Corresponding Secretary
Mrs. Neil Russo, Litchfield
Treasurer
Mrs. David Peterson, New London

PRESIDENT'S ANNUAL REPORT—1971-1972

It has been a busy, and I hope profitable year. Starting with the national convention in Atlantic City in June, it moved on to board meetings in June, September, November, February and April. A national conference in Chicago in October was followed by a workshop in Pittsburgh. Early in November we held our own state workshop which was well attended and rather enjoyed. Round table discussion groups met on AMA-ERF, Legislation, and Membership. Our semi-annual meeting was held in Waterbury on October 26th. In January, through the generous support of the Connecticut State Medical Society, we were able to enclose an extra page in *Connecticut Medicine* promoting membership. Since 1972 marks the 50th birthday of the Woman's Auxiliary to A.M.A., national has set its goal at 100,000 members. It is difficult to report accurately on the results of this since some of the counties are holding new memberships rather than rebilling in a few months. For instance, Hartford County is holding dues of fifteen women who will be received as full members in June. It is more and more evident that there are qualified doctors who do not belong to the Society, and because of this their wives are not eligible to belong to the county auxiliaries. To them, let us say they are missing much in the way of information. We feel they are failing to give the valuable contribution they have to offer. Our drive for new members extends through 1972.

On February 8th, under the direction of Mrs. Ronald Beckett, Hartford County sponsored a "School Day" program for the education of all doctors' wives—to bring them up to date on what is taking place in medicine today and what is ahead for medicine. 150 attended. The morning session was one of basic instruction conducted by Dr. Benjamin Wiesel and Dr. Sidney Cramer. The afternoon session presented the viewpoints of protagonists of different groups. The program was moderated by Dr. Weisel. A somewhat similar program, moderated by Dr. Thomas Masterson was held in New London County.

There seems to be a growing movement to present the image of the physician to the public in a sympathetic yet constructive way. In Windham County two radio stations have given time for a monthly show on "Meet Your Doctor" at which time local health problems are discussed by a physician and a moderator. Some Auxiliary activities not realized in the state are: the Auxiliary has been represented on COMPAC, the Public Affairs Committee of Connecticut State Medical Society, we have had three members on the state Health Council, two on the Governor's Commission on School Health, two on the Connecticut Nutrition Council. These are all key positions in the state, and cannot be lost. In Legislation the names of 42 auxiliary members who have volunteered to attend state legislation hearings in support of Medical Society sponsored bills has been filed at the State Office.

I say to you today that the cancer gnawing at our vitality is apathy, and indifference to what lies ahead for medicine. In this election year we can ill afford not to become involved.

We can promise people help, and give families food stamps to combat hunger, but unless we help educate and employ these people we will repeat the pattern in the next generation. We can promise full health care but unless we educate people to individual responsibility for their own health, the problem will not be solved. The major killers are tied to personal responsibility, for example the relationship of diet and exercise to heart disease, judgment to accidents; and smoking and air pollution to lung disease.

We can promise states help and return tax money to them, but we must also see to it they use the funds equitably and efficiently. We can give candidates and a party support, but we must also see to it that there is a follow-through on promises. We can be successful in lobbying for legislation, but we should not then ignore how it is implemented.

It is imperative that we work together to urge that all health legislation not be pie-in-the-sky promises but something that can be delivered, using the resources available in numbers of physicians and facilities, with an assurance of *quality* medical care for *all*.

I received the latest information today that the Woman's Auxiliary in Connecticut during the past year has contributed $3,100. to AMA ERF, and money is still coming in.

Mrs. Forrest Gibson, *President*

np

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Welcome, New Members

Fairfield County

Vincent Annunziata, M.D., Fairfield Hills Hospital, Newtown, Connecticut 06470.

Robert L. DeBernardo, M.D., 3915 Main Street, Bridgeport, Conn. 06605.

Gary A. Gallo, M.D., 49 Lake Avenue, Greenwich, Conn. 06830.

James V. Halloran, M.D., Greenwich Hospital Association, Greenwich, Conn. 06830.

Carlos E. Hansen, M.D., 1799 Summer Street, Stamford, Conn. 06902.

Sarah L. Jonas, M.D., 12 Timber Top Trail, Wilton, Conn. 06897.

James G. Katis, M.D., Silver Hill Foundation, New Canaan, Conn. 06840.

Nicholas Kopeloff, M.D., 4 Dearfield Road, Greenwich, Conn. 06830.

Marvin L. Lewin, M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.

Stephen H. Lewis, Jr., M.D., 8 West End Avenue, Old Greenwich, Conn. 06870.

Mohamed Mujeeb, M.D., 29 Hoyt Street, Stamford, Conn. 06905.

Robert D. Newman, M.D., Greenwich Hospital, Greenwich, Conn. 06830.

George D. Schare, M.D., 340 Capitol Avenue, Bridgeport, Conn. 06606.

William C. Spring, Jr., M.D., 180 Bayberry Lane, Westport, Conn. 06880.

Litchfield County

Graham B. Blaine, Jr., M.D., Housatonic Psychiatric Center, Box 153, Lakeville, Conn. 06039.

John P. Curtis, M.D., Sharon Clinic, Sharon, Conn. 06069.

Samuel W. Moore, M.D., Cottage Low Road, Sharon, Conn. 06069.

Carl Tunick, M.D., 18 Elm Street, New Milford, Conn. 06776.

Middlesex County

Edward J. Bernacki, M.D., 410 Sheriden Drive, Cheshire, Conn. 06410.

Joseph A. Donadio, M.D., 151 Deer Lane, Guilford, Conn. 06437.

Joseph P. Fiducia, M.D., 80 South Main Street, Middletown, Conn. 06457.

Prabhash C. Ganguli, M.D., 28 Crescent Street, Middletown, Conn. 06457.

Charles F. Rich, M.D., 24 In Town Terrace, Middletown, Conn. 06457.

New London County

John H. Baker, M.D., Naval Submarine Medical Center, Groton, Conn. 06340.

Ralph A. Bolstad, M.D., Norwich State Hospital, Norwich, Conn. 06360.

C. Albert Kim, M.D., Lawrence & Memorial Hospitals, New London, Conn. 06320.

Samuel T. Glasser, M.D., 4 Columbus Avenue, Niantic, Conn. 06357.

Melvin A. Yoselevsky, M.D., 334 Montauk Avenue, New London, Conn. 06320.

Daniel D. Young, M.D., Uncas-on-Thames, Norwich, Conn. 06360.

State Physicians Art Group Awards Prizes

The Connecticut Physicians' Art Association 1972 exhibit was held April 25, 26 and 27 in conjunction with the 180th annual meeting of the Connecticut State Medical Society at the Hartford Hilton Hotel.

The "Best in Show" award was given to Margaret Hayes, wife of Dr. Mark Hayes, Hamden, for her oil painting "The Big Apples" and the John M. Freiheit award, given by the New Haven County Medical Association, went to Dr. William Schneider of Rockville for his oil painting "Bandanna".

In the professional class in watercolor, Tibor de Cholnoky, M.D. of Greenwich won first for "Woodstock Farm" with Mrs. Paul McAlenney of Woodbridge, second for "Morning of the Race", and Dr. Cholnoky, of Greenwich, Honorable Mention for "Just Flowers". Dr. Sophie Trent, of Meriden, received a first prize for her "Solitude" in mixed media. Professional oil winners were: first award to Mrs. Morton Opinsky, West Hartford for "The Shuttered Window", and second, Ruth Waskowitz, wife of David Naskowitz, M.D., New Britain, for her portrait of "Susan".

In the intermediate group, Eleanor Anderson, West Hartford, wife of Albin Anderson, M.D., received a first award for her acrylic "Still Life", Carol Sirot, New Haven, wife of Gustave Sirot, M.D., second for "Fire", and Barbara Olson, North Haven, wife of Lowell Olson, M.D. received Honorable Mention for her oil portrait. Robert Lowman, M.D., also of North Haven, won a first award for his black and white drawing "Untitled" and Elliott Brand, M.D., New Haven, a first for his colored floral photograph.

Frances Kim, wife of Kisik Kim, M.D., New Haven, was awarded first prize for her metal sculpture in the professional class, entitled "Symphony" and Allen B. Silberstein, M.D., Portland, a first for "Lighthouse" etching in slate, with Sylvia Campbell-Jacobs, Middle Haddam, wife of R. Campbell-Jacobs, M.D. for her stoneware pottery.

In the childrens group, the first award went to Pamela Westerfield, Hamden, granddaughter of Orvan W. Hess, M.D., for her guache painting "Alice's Toadstools", second to Jeffrey Miller, Haddam, son of Dr. Donald Miller, for his pastel drawing, and honorable mention to his sister, Natalie Miller, for her poster paint drawing.

The co-chairmen of the exhibit were Eugene Rightmyer, M.D., President of the Connecticut Physicians' Art Association and Mrs. Orvan W. Hess, Vice-President, assisted by Mrs. Albin Anderson and Mrs. Lowell Olson, Art co-chairmen for the Woman's Auxiliary to the Connecticut State Medical Society.

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NEW BOOKS IN REVIEW

FABRICATED MAN: THE ETHICS OF GENETIC CONTROL. Paul Ramsey. Yale University Press, 1970. 174 pp. $7.50.

Reviewed by: LOUIS H. NAHUM

In this book the author first presents a brief review of the evidence for man's impending genetic deterioration. He next examines which of the various present and possible scientific developments to combat this assumed deterioration are ethically acceptable within the framework of his concept of Judeo-Christian morality. His position is clear: "Men ought not to play God before they learn to be men and after they have learned to be men they will not play God" (p. 138).

Man begins to play God with those proposals which "would irreversibly remove a basic form of humanity: "the basis in our creation for the covenant of marriage and parenthood" (p. 1301). Thus he finds voluntary control of parenthood based on genetical knowledge acceptable including early abortion as the grounds of grave defect. But he finds artificial insemination as the basis for a desire for a superior child or cloning unacceptable on the ground that the amitive and procreative aspects of human sexuality are morally unseparable.

Genetic surgery is in theory acceptable but he does not see how we can ethically traverse the necessary period of human experimentations "because we ought not to choose for a child whose procreation we are contemplating, the injury he may bear. There is no way by which we can morally get to know whether many things now planned are technically feasable or not (p. 134).

Although, the theological argument is clearly central, he recognizes the other perplexing decisions related to these possible developments: who in this rapidly changing world would be a superior sperm donor? What might be the unanticipated psychological problems of the cloned, etc? He develops his case logically, clearly and forcibly.

What to most geneticists would be the most conservative "next" development: germinal choice through artificial insemination is to him far more unethical than the genetically more controversial "genetic purges" (granted the solution of technical problems). Professor Ramsey's challenge to what he sees as the new biological morality is clear and deserves not to go unheeded.

PREVENTIVE MEDICINE IN WORLD WAR II, VOL. IX, SPECIAL FIELDS. Washington, D.C., Office of the Surgeon General, 1969. Price not given.

Reviewed by HERBERT LEVINE

This volume represents a return to the dry, tedious, and exhaustive type of presentation that one had come to expect from this series of military medical memorabilia. The last one presented to this Journal for review was "Crisis Fleeting", a series of personal reminiscences of the CBI Theater in World War II that made for fascinating reading, and was also the subject of considerable controversy in the pages of one of the free periodicals distributed to physicians.

This book, subtitled "Special Fields", consists of sections devoted to training, health education, industrial medicine, heat and cold injuries, medical intelligence, prisoners of war, and medical laboratories. Each section is replete with tables, lists, etc., that are certainly comprehensive but far from interesting. The material regarding heat and cold injuries is clinically scant, and has been updated many times since World War II elsewhere.

This book has little to offer the reader, but it may be useful to persons requiring the highly specialized historical data it contains.

NEUROHYPOPHYSIAL HORMONES, CIBA Study Group #39, edited by G. E. W. Wolstenholme and Joan Birth, Churchill Livingstone, Edinburgh and London, 1971. 146 pages, 34 illustrations.

Reviewed by: M. NATHAN LASSMAN, M.D.

This monograph, a symposium in honor of Hans Heller, deals primarily with the physiology and evolution of the neurohypophysial hormones. One third of the book pertains to argine vasotocin, a hormone not present in man. A chapter by K. Lediris et al discusses exocytosis as a mechanism of hormone release and is accompanied by electron-micrograph reproductions and a discussion of their significance in elucidating the mechanism of hormone release. Evidence biochemically confirming neurosecretion of oxytocin and vasopressin and intraneural transport is presented with a good review by B. T. Pickering, C. W. Jones and S. D. Burford. The chapter concerned with regulation of the anterior pituitary is already out of date with little discussion about thyroid releasing factor which has been synthesized and used in several studies reported in recent American literature, and LH releasing factor, which has been extracted from blood and median eminence. There is little discussion about each of the pituitary hormones and specific areas in the hypothalamus of mammals implicated in their control.

In summary, this is a monograph dealing with hormone action primarily in non-mammals, with some discussion of hormone synthesis, transport and release. For the scientist interested in this area, it is a useful review.

NEW BOOKS RECEIVED

A Decade of Progress. The United States Army Medical Department 1959-1969. Prepared and published under the direction of Lieutenant General Hal B. Jennings, Jr., The Surgeon General, United States Army. Editor in Chief, Colonel William S. Mullins, MSC, USA. Editor for *A Decade of Progress,* Rose C. Engelman, Ph.D. Office of the Surgeon General, Department of the Army, Washington, D.C., 1971. 214 pp. $2.25 per copy from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

LACTOGENIC HORMONES. A Ciba Foundation Symposium in memory of Professor S. J. Folley. Edited by G. E. W. Wolstenholme and Julie Knight. Churchill Livingstone, Edinburgh and London, 1972. pp. 404.

Reviewed by: LEON SPEROFF

The Ciba Foundation owes its existence to the generosity of CIBA Ltd., but its activities are independently guided by a group of trustees, who organize frequent symposia for the sole purpose of scientific communication. One has come to expect excellence in the published volumes of these symposia, and this volume is not disappointing.

The breast is the most unique feature of reproduction in the group of animals known appropriately as mammals. This late development in the evolutionary scheme is, as one might expect, very complex in its growth and function. The requirements of milk production are truly excessive, requiring contributions from many of the body's hormones, but the foundation for lactation is prolactin.

There is no longer any doubt that prolactin exists; it is not growth hormone or part of the growth hormone molecule. Prolactin is a polypeptide secreted from the anterior pituitary, and has a half life of 15-30 minutes.

The chapter by R. W. Turkington on the Molecular Biological Aspects of Prolactin is expecially clear and lucid. Turkington has developed an *in vitro* model to explore the mechanism of prolactin action and mild production. Delightful and fascinating discussions (arguments) can be found after most of the chapters, but the flavor of the symposium can be best appreciated in the discussion following Turkington's chapter—a controversy over whether prolactin is a growth hormone for the mammary gland, between Meites (yes) and Turkington (no).

Whether galactorrhea occurs or not, prolactin is uniformly elevated in patients receiving therapeutic amounts of the tranquilizer drugs. An unanswered question is whether breast carcinoma is more common in women on tranquilizers. One would hope that Turkington is right and prolactin is not growth promoting. Initial studies have not revealed a correlation between prolactin levels and the clinical course of patients with carcinoma of the breast, and *in vitro*, Turkington can not show stimulation of DNA synthesis by prolactin.

An excellent summary of the hypothalamic-pituitary axis control of prolactin secretion can be found in the chapter by J. Meites.

Recently it has been suggested that a stimulating factor, PRF, may also exist. Birds are known to be regulated by PRF rather than PIF, while rat median extracts possess some stimulatory capability or prolactin secretion. In addition, suckling rats do not show a decrease in the hypothalamic content of PIF. Nicoll suggests that PRF may regulate the pool size of prolactin and PIF control turnover rate by controlling release.

Approximately half of patients with idiopathic galactorrhea develop pituitary tumors. However, not all patients with galactorrhea will have elevated prolactin levels.

L-dopa can cross the blood-brain barrier and be decarboxylated to dopamine thereby stimulating PIF and decreasing galactorrhea. Success with L-dopa treatment has been variable, but upon withdrawl of L-dopa, prolactin levels have always increased and galactorrhea returned. Ergo, drugs also inhibit prolactin secretion, perhaps directly at the pituitary level, but clinical experience is not sufficient to assess success vs. side effects.

In the future, synthesis of PIF itself may provide us with the best method of treatment for galactorrhea.

Finally, it should be mentioned that the structure, function, and secretion of human placental lactogen (or human chorinoic somatomammotropin according to the new terminology) are discussed, and it is apparent that the physiological role for this hormone remains to be determined.

Science News

An "Artificial" Muscle To Replace The Heart

(*Heart Research Newsletter* 16:2, Winter, 1971.) Dr. Philip N. Sawyer and his colleagues have built a one-chambered device patterned after the left ventricle made of temperature sensitive alloy of nickel and titanium dubbed nitinol. This alloy abruptly contracts when heated beyond a critical or transitional temperature and just as swiftly expands or relaxes when allowed to cool below this point. The hot-cold switching is accomplished electrically by passing electric current through the alloy to heat it up beyond a critical temperature.—L.H.N.

Influenza In England And Wales

(*Lancet* I:193, January 22, 1972.) In the week ended January 7, influenza deaths rose for the fourth week in succession to 180 compared with 87 the previous week. The corresponding week last year showed 33 deaths.

An increasing number of isolations of the Hong Kong variant of influenza A_2 virus are being reported in different parts of the country by the Public Health Laboratory Service.—L.H.N.

Iron And Vitamin C

(*Lancet* II, 768, October 2, 1971) One of the more important factors which influence red cell formation in iron deficiency anemia is the degree of saturation of the labile-ascorbic acid pool. A relative shortage of either ascorbic acid or iron will interfere with optimal hemoglobin synthesis.

There is an increased demand for ascorbic acid when iron is administered to elderly women and men. To treat iron deficiency anemia it is thus necessary not only to give iron but also increased amounts of vitamin C.–L.H.N.

Connecticut Medicine

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